Southern Medical Journal

JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

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Southern Medical Journal

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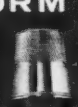

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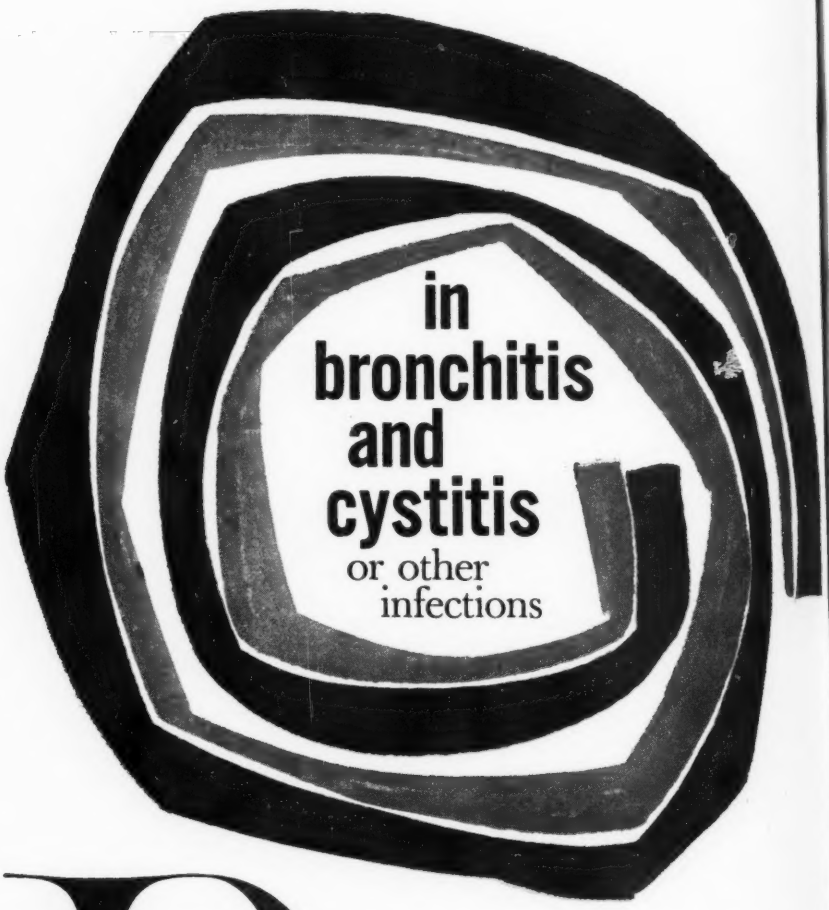

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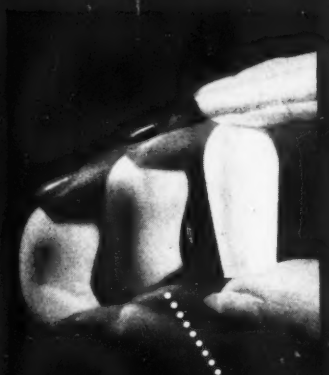

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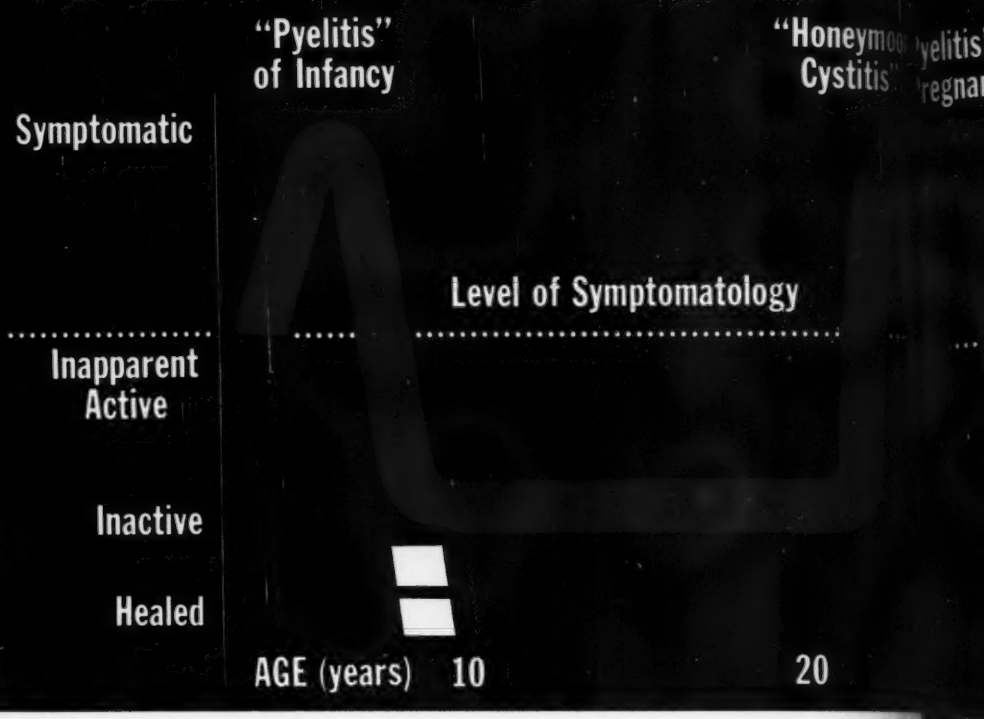

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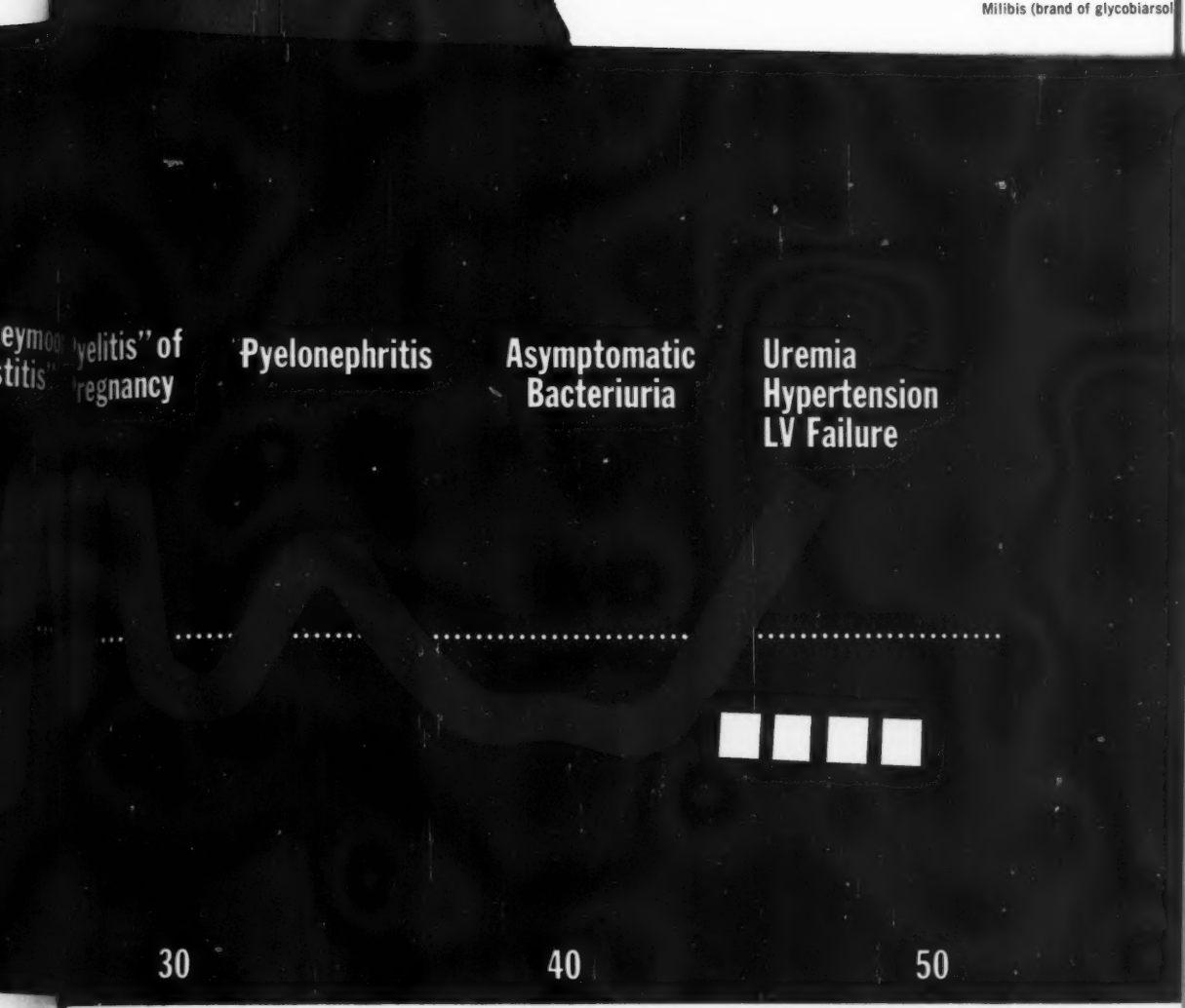

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1. Birchall, R.: Am. Practit. *11*:918, 1960. 2. Sanjurjo, L. A.: Med. Clin. N. Amer. *43*:1601, 1959.

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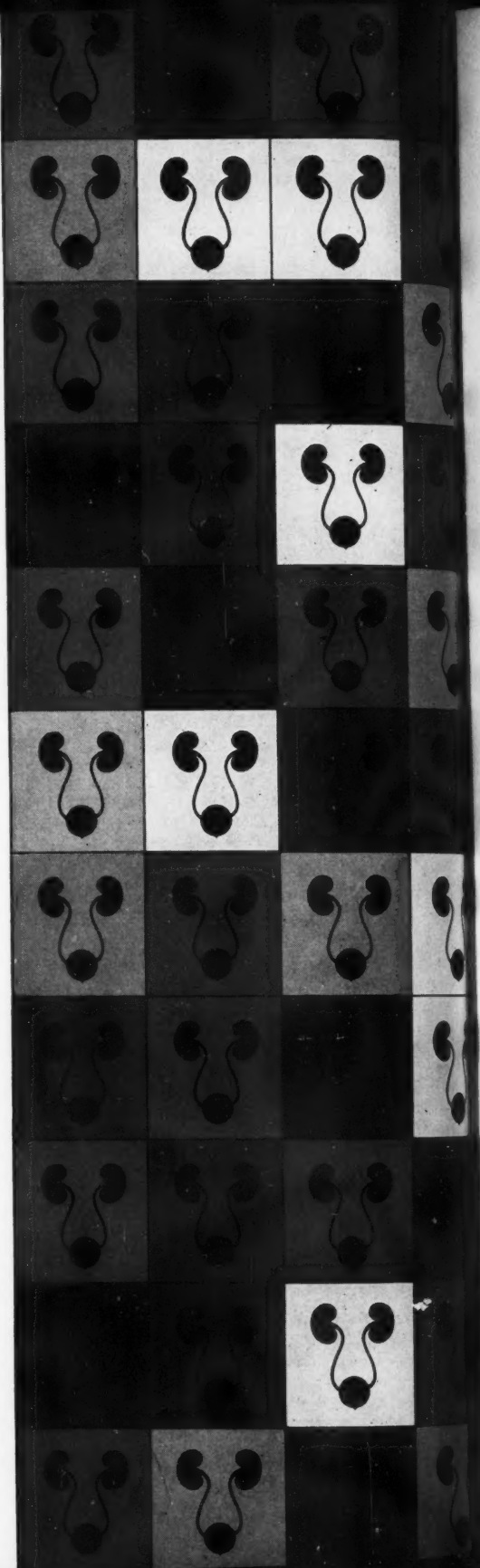

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References: 1. Bourque, J.-P., and Gauthier, G-E.: L'Union Medicale **89**:840 (May) 1960. 2. Cottrell, T. L. C., Rolnick, D., and Lloyd, F. A.: Rocky Mountain M. J. **56**:66 (Mar.) 1959. 3. Bourque, J.-P., and Joyal, J.: Canad. M.A.J. **68**:337 (Apr.) 1953. 4. Hughes, J., Coppridge, W. M., and Roberts, L. C.: North Carolina M. J. **17**:320 (July) 1956.

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Many of your arthritic patients, too, can wake up comfortable on Medrol Medules.

Dosage: The following dosages are recommended in rheumatoid arthritis:

	Initial	*Maintenance*
Severe	12 to 16 mg.	6 to 12 mg.
Moderately severe	8 to 10 mg.	4 to 8 mg.
Moderate	6 to 8 mg.	2 to 6 mg.
Children	6 to 10 mg.	2 to 8 mg.

With Medrol Medules, it may be possible to reduce the total daily dose by ½.

Indications and effects: Medrol benefits (anti-inflammatory, antiallergic, antirheumatic, antileukemic, antihemolytic) have been demonstrated in acute rheumatic carditis, rheumatoid arthritis, asthma, hay fever and allergic disorders, dermatoses, blood dyscrasias, and ocular inflammatory disease involving the posterior segment.

Precautions and contraindications: Because of Medrol's high therapeutic ratio, patients usually experience dramatic relief without developing such possible steroid side effects as gastrointestinal intolerance, weight gain or weight loss, edema, hypertension, acne, or emotional imbalance.

As in all corticotherapy, however, there are certain cautions to be observed. The presence of diabetes, osteoporosis, chronic psychotic reactions, predisposition to thrombophlebitis, hypertension, congestive heart failure, renal insufficiency, or active tuberculosis necessitates careful control in the use of steroids. Like all corticosteroids, Medrol is contraindicated in patients with arrested tuberculosis, peptic ulcer, acute psychoses, Cushing's syndrome, herpes simplex keratitis, vaccinia, or varicella.

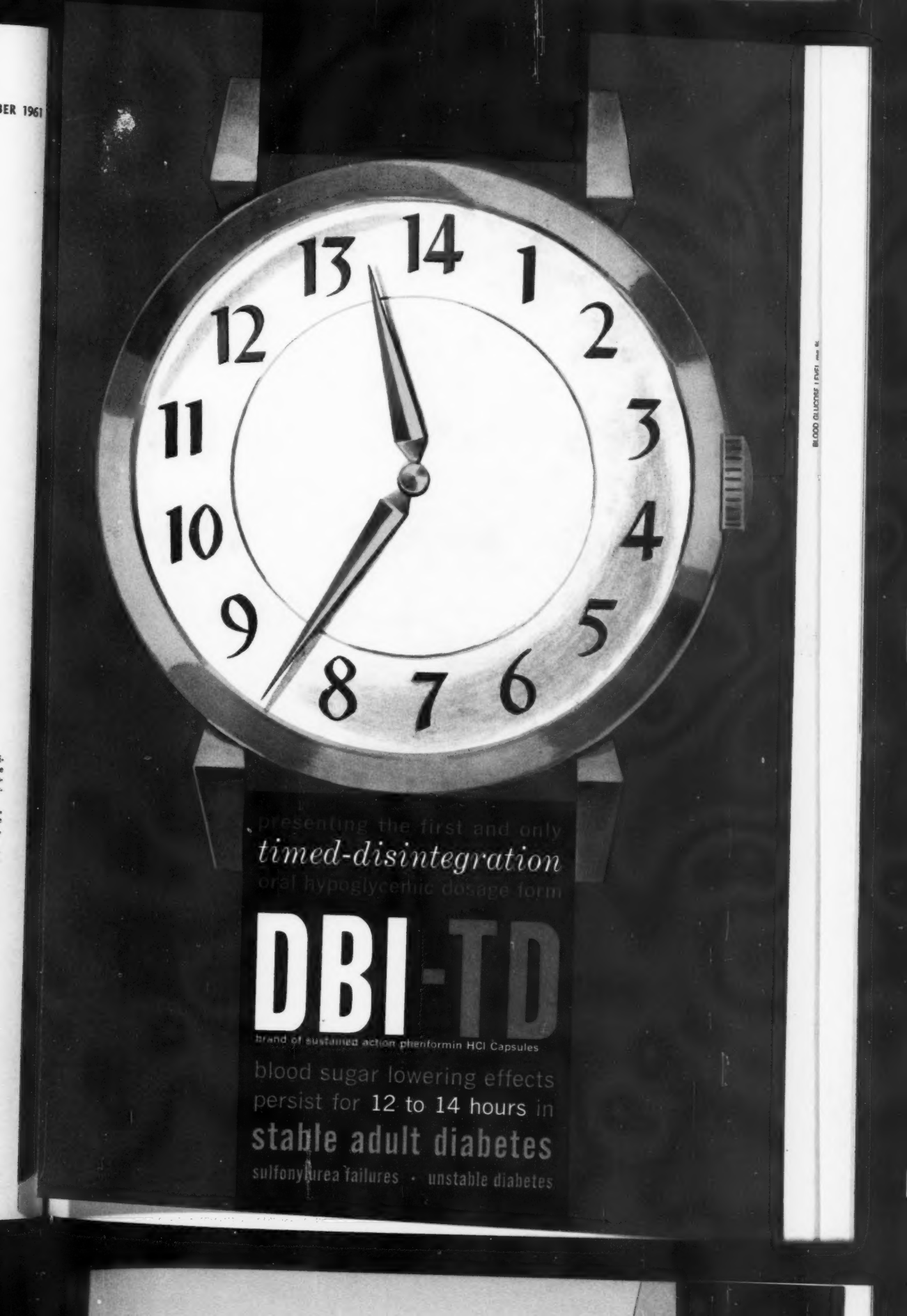
Approximately 135 tiny "doses" mean smoother steroid therapy

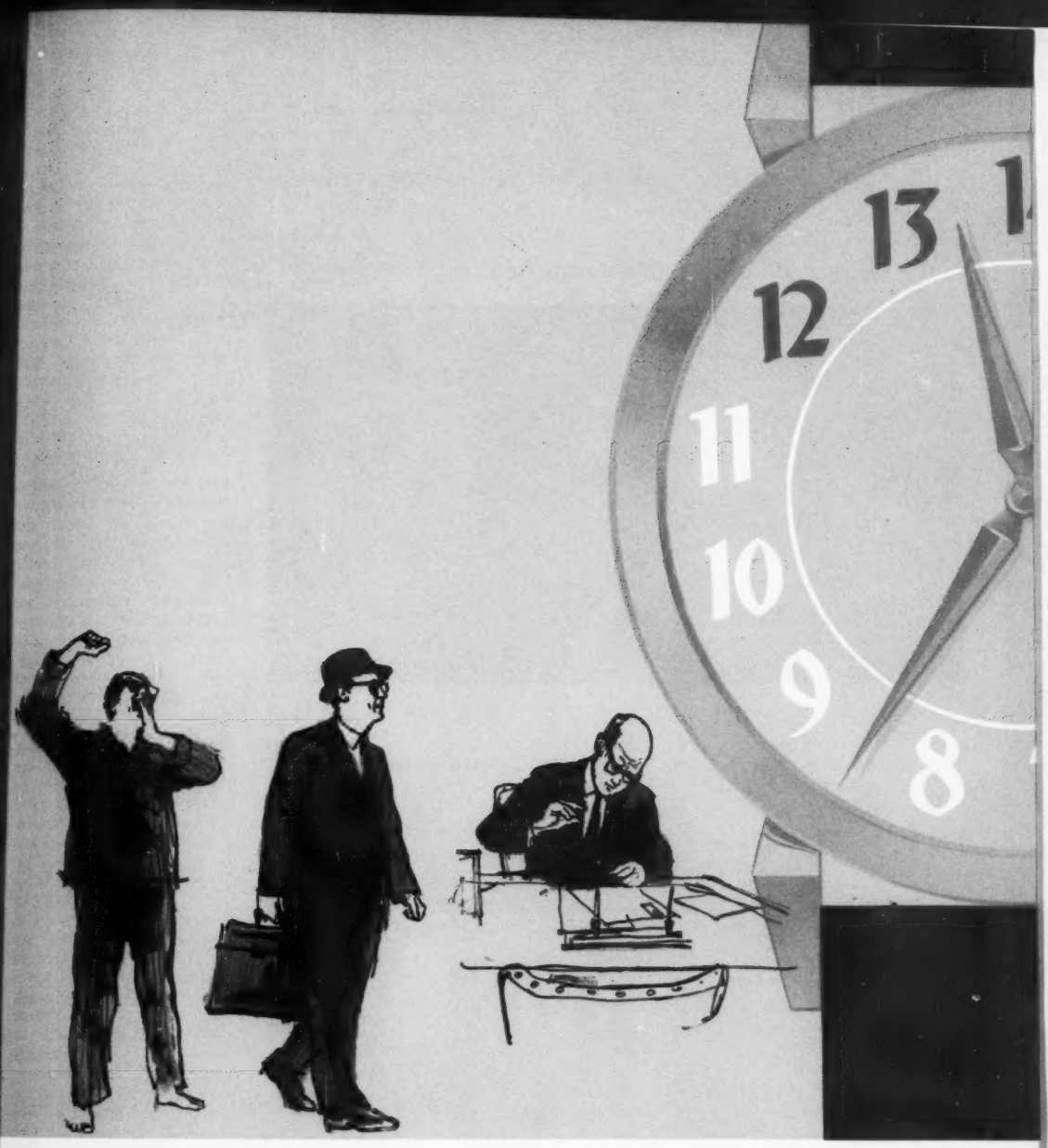
Medrol* Medules*

Each capsule contains: Medrol (methylprednisolone) 2 mg. or 4 mg.
Supplied in bottles of 30 and 100.

Upjohn

*TRADEMARK, REG. U.S. PAT. OFF. COPYRIGHT ©1961, THE UPJOHN COMPANY JUNE, 1961 THE UPJOHN COMPANY, KALAMAZOO, MICHIGAN


presenting the first and only
timed-disintegration
oral hypoglycemic dosage form
DBI-TD
brand of sustained action phenformin HCl Capsules
blood sugar lowering effects
persist for 12 to 14 hours in
stable adult diabetes
sulfonylurea failures · unstable diabetes



the advantages of phenformin and sustained action are combined in

DBI®-TD

CAPSULES 50 mg.

...approaches the ideal in oral therapy for stable adult diabetes

each dose lowers blood sugar levels for about 12 to 14 hours

convenient—one dose a day, or two at most, for a great majority of patients

well tolerated... minimal g.i. side effects

virtually no secondary failures in stable adult diabetes

no liver or other clinical toxicity after up to 2½ years of daily use of DBI-TD (nearly 5 years with the DBI tablet)

NOTABLE RECORD OF CLINICAL EFFICACY

in stable adult diabetes up to 88% respond to phenformin.[1,17] "In our experience the action of DBI on the adult stable type of diabetes is impressive."[1] "There is... a virtual absence of acquired resistance or true secondary failure."[8]

in sulfonylurea failures (primary and secondary) therapy with DBI-TD Capsules[3] results in control of a majority of patients.

in labile diabetes DBI-TD Capsules,[5,6,16] as adjunct to injected insulin, often improve regulation of the diabetes.

NOTABLE RECORD OF CLINICAL SAFETY

No clinical toxic effects on the liver, kidney, or blood due to DBI-TD Capsules or DBI Tablets have been reported[7,8,9,10] following daily use in diabetics for varying periods up to 4½ years.[8] "The absence of hypoglycemic reactions has been conspicuous."[14]

DBI-TD Capsules are substantially well tolerated by the gastrointestinal tract[11,12,13,16,17] when administered as directed.

NOTABLE DOSAGE SIMPLICITY, CONVENIENCE, LOW COST

Once-a-day dosage — or at most twice-a-day — makes DBI-TD simple and convenient therapy. Maintenance dosage is readily established and adjustments are infrequently required in the ketosis-resistant patient.

"more convenient, more effective and better tolerated"

lets

ic

rated
en

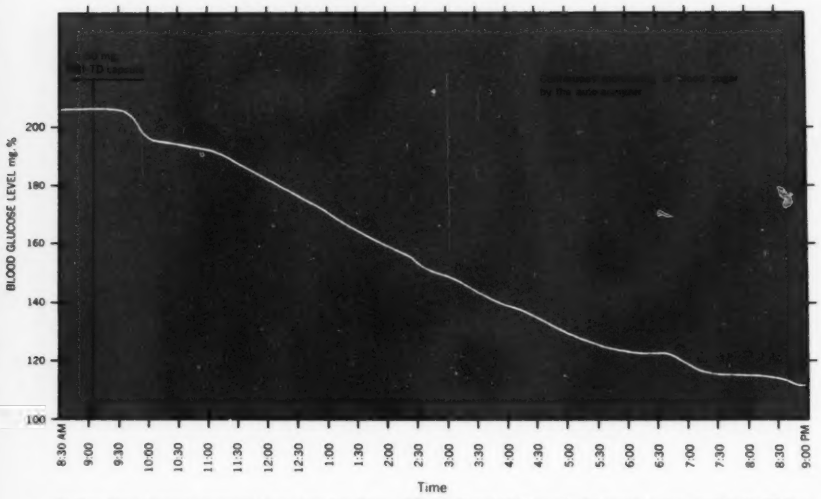
LOW COST
y —
apy.
and

"more convenient, more effective and better tolerated."

DBI-TD—the new convenient and well-tolerated Timed-Disintegration capsule form of DBI—further simplifies effective control of a great majority of diabetics.

Phenformin is believed to exert its hypoglycemic effects primarily by promoting cellular metabolism of glucose via the physiologic Embden-Meyerhof glycolytic pathway.

a single dose of DBI-TD lowers blood sugar for 12 to 14 hours[10,11,12,15]



12-Hour Hypoglycemic Response Curve after One 50 mg. DBI-TD (Timed-Disintegration) Capsule in Fasting Diabetic (Weller)

1. Walker, R. S.: Brit. M. J. 2:405, 1959. 2. Hamel, J. F.: Applied Therapeutics 2:137, 1960. 3. Moss, J. M., DeLawter, D. E., Tyroler, S. A., and Field, J. B.: Med. Times 89:561, 1961. 4. Krall, L. P.: Applied Therapeutics 2:137, 1960. 5. Craig, J. W.: Personal communication. 6. White, P. and Krall, L. P.: Personal communication. 7. Miller, E. C., and Roller, G. W.: Med. Times 89:196, 1961. 8. Pomeranze, J.: Clinical Medicine 8:1155, 1961. 9. Barclay, P. L.: J.A.M.A. 174:474, 1960. 10. Krall, L. P.: Med. Clinics N.A. In press. 11. Radding, R. S., and Zimmerman, S. J.: Metabolism 10:238, 1961. 12. Beaser, S. B.: Personal communication. 13. Gurol, F.: Personal communication. 14. Pearlman, W.: Phenformin Symposium, Houston, Feb. 1959. 15. Weller, C., and Linder, M.: Metabolism 10:699, 1961. 16. Fabrycant, M. and Ashe, B. I.: Metabolism 10:684, 1961. 17. Radding, R. S., McHenry, J. I., Neely, W. B., and Lummis, F. R.: Presented at Fourth Congress of Internat. Diabetes Fed., Geneva, June 1961.

DBI-TD (brand of Phenformin HCl—N[1]-β-phenethylbiguanide HCl) available as 50 mg. timed-disintegration capsules; bottles of 100 and 1000 capsules. Also available as DBI tablets, 25 mg., bottles of 100 and 1000.

DBI-TD

CAPSULES 50 mg.

u. s. vitamin & pharmaceutical corporation

Arlington-Funk Laboratories, division • 800 Second Ave., New York 17, N. Y.

administration and dosage: One 50 mg. DBI-TD capsule with breakfast regulates many stable adult diabetics. If higher dosages are needed, a second DBI-TD capsule is added to the evening meal, and further increments (at weekly intervals) to either the A.M. or P.M. dose. In patients requiring insulin, reduction of insulin dosage is made as DBI-TD dosage is increased, until effective regulation is attained. (The acidosis-prone, insulin-dependent diabetic should be closely observed for "starvation" ketosis.) Sulfonylurea secondary failures usually respond to relatively low dosages of DBI-TD alone, or combined with reduced dose of sulfonylurea.

side effects: Gastrointestinal reactions occur infrequently and are usually associated with higher dosage levels. They may include unpleasant, metallic taste in the mouth, continuing to anorexia, nausea, and, less frequently, vomiting and diarrhea. They abate promptly upon reduction of dosage or temporary withdrawal. In case of vomiting, DBI-TD should be withdrawn immediately.

precautions: Particularly during the initial period of dosage adjustment, every precaution should be observed to avoid acidosis and coma or hypoglycemic reactions. Hypoglycemic reaction has been observed on rare occasions in the patient treated with insulin or a sulfonylurea in combination with DBI-TD. "Starvation" ketosis, that is the appearance of acetonuria in the presence of a lowered or normal blood sugar, must be distinguished from "insulin-lack" ketosis which is accompanied by hyperglycemia and acidosis. A reduction in the dose of DBI-TD of 50 mg. per day (with a slight increase in insulin as required), and/or a liberalization in carbohydrate intake rapidly restores metabolic balance and eliminates the "starvation" ketosis. Do not increase DBI-TD dosage or give insulin without first checking blood and urine sugars.

caution and contraindication: As with any oral hypoglycemic therapy reasonable caution should be observed in severe preexisting liver disease. The use of DBI-TD **alone** is not recommended in the acute complications of diabetes: acidosis, coma, infections, gangrene or surgery.

Complete detailed literature is available to physicians.

Calms the Tense, Nervous Patient

in anxiety and depression

The outstanding effectiveness and safety with which Miltown calms tension and nervousness has been clinically authenticated by thousands of physicians during the past six years. This, undoubtedly, is one reason why meprobamate is still the most widely prescribed tranquilizer in the world.

Its response is predictable. It will not produce unpleasant surprises for either the patient or the physician. Small wonder that many physicians have awarded Miltown the status of a proven, dependable friend.

Miltown®
meprobamate (Wallace)

Usual dosage: One or two 400 mg. tablets t.i.d.
Supplied: 400 mg. scored tablets, 200 mg. sugar-coated tablets; bottles of 50. Also as MEPROTABS®—400 mg. *unmarked*, coated tablets; and in *sustained-release* capsules as MEPROSPAN®-400 and MEPROSPAN®-200 (containing respectively 400 mg. and 200 mg. meprobamate).

WALLACE LABORATORIES
Cranbury, N. J.

CM-5642

Clinically proven in over 750 published studies

1. Acts dependably — without causing ataxia or altering sexual function
2. Does not produce Parkinson-like symptoms, liver damage or agranulocytosis
3. Does not muddle the mind or affect normal behavior

WITH THE TIDE OF MEDICAL THINKING

Concern about changing bacterial sensitivity
Madribon controls even some antibiotic-resistant organisms

Concern about safety and tolerance
Madribon has a safety record unchallenged by any antibacterial agent

Concern about economy and ease of therapy
Madribon is "kind to the purse"; need be given only once a day

Madribon

for respiratory tract infections

Consult literature and dosage information, available on request, before prescribing.

MADRIBON®—2,4-dimethoxy-6-sulfanilamido-1,3-diazine
ROCHE
LABORATORIES • Division of Hoffmann-La Roche Inc.

ARMOUR PHARMACEUTICAL COMPANY
ANNOUNCES THE FIRST SELECTIVE TENSITROPIC

L I S T I C A®

I am pleased to inform you of the latest development in our Company's continuing research for superior chemotherapeutic agents.

For patients suffering from tension/anxiety states, we are offering the medical profession Listica— a new and selectively different monocarbamate. Frankly, we would be hesitant about entering a field already crowded with good drugs were it not for the marked differences Listica presents.

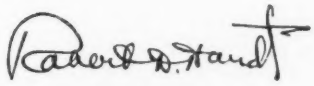
Listica is **not** "just another tranquilizer." We, therefore, call it **The First Selective Tensitropic**. Here are the reasons why:

New Listica allays tension/anxiety in as many as 89% of cases by selectively inhibiting impulses through internuncial pathways of the central nervous system. However, it does not affect the unconditioned response; thus, Listica does not induce apathy or impair acuity.

The past three and one-half years of clinical studies have demonstrated the safety and efficacy of Listica in 1,759 patients. There have been **no reports of contraindications, toxicity, habituation or serious side effects.**

One tablet q.i.d. is adequate dosage to allay tension/anxiety, maintain acuity, and promote **eunoia** *—"a normal mental state." This simple, effective dose remains the same, even in maintenance therapy.

We are sending you samples and published clinical reports on Listica. We will be happy to send you a copy of the first "Symposium on Hydroxyphenamate" on request. I believe you will find Listica a valuable addition to the arsenal of chemotherapeutics for combatting tension/anxiety in your practice.



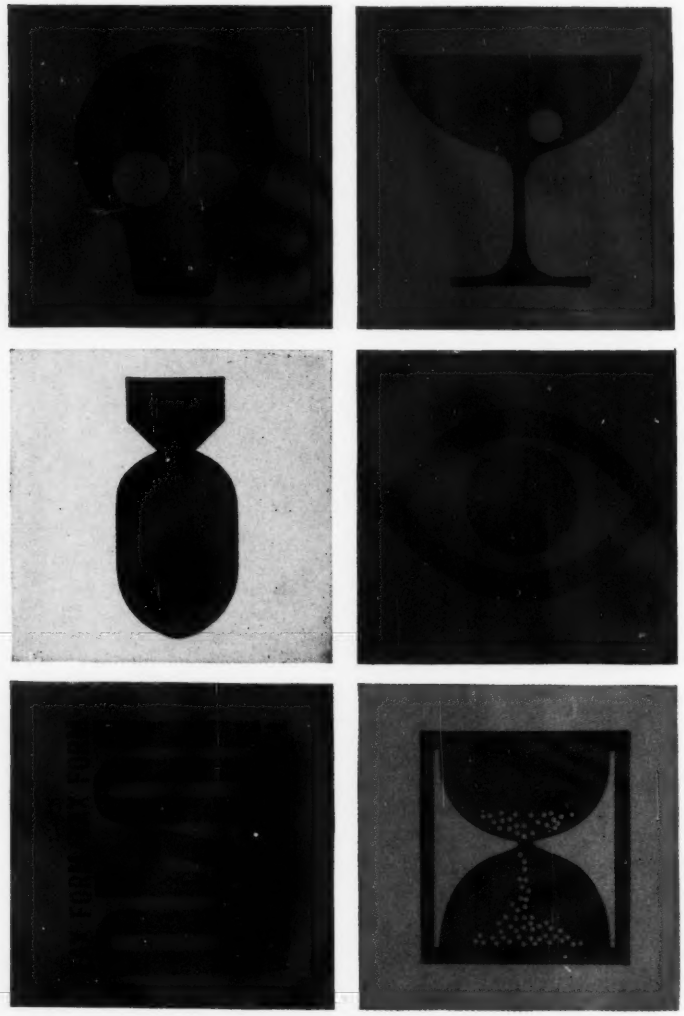
Robert A. Hardt, President

P.S.: Physicians who prefer generic names prescribe "Hydroxyphenamate, Armour."

LISTICA—Hydroxyphenamate, Armour. © 1961, A.P. CO. *Stedman's Medical Dictionary.

ANNOUNCING THE FIRST

Symbols of the Age of Tension/Anxiety



LISTICA by ARMOUR

allays TENSION/ANXIETY...
maintains acuity... promotes eunoia*...
facilitates somatic diagnosis and therapy

T

SELECTIVE TENSITROPIC
LISTICA®

lifts the facade of TENSION/ANXIETY New Listica allays tension/anxiety in as many as 89% of cases,[2-13] by selectively inhibiting impulses through internuncial pathways of the central nervous system. Whether the patient's tension/anxiety is psychosomatic or a complication of somatic disorder, Listica reduces or eliminates the excess impulsivity seen in tension/anxiety states.

maintains normal acuity Unlike many drugs, Listica does not affect unconditioned response or normal motor activity. Thus, Listica allays tension and anxiety without inducing apathy or impairing acuity; patients are able to pursue normal activities, such as driving, reading, writing, etc., without interference from drug therapy.

enhances physician-patient rapport As it removes tension/anxiety, fear and frustration, **LISTICA PROMOTES EUNOIA***—"a normal mental state." It bares the patient's true somatic condition, and facilitates diagnosis and therapy. Patients are more tractable to concomitant drug therapy, respond better, faster.

without known toxicity or contraindications Listica is safe, as well as effective. Chronic studies[14] in rats (12 months) and dogs (6 months) were free of toxic manifestations at oral dosage levels as high as 200 mg./kg./day (approximately 10 times the recommended human dosage). No macroscopic or microscopic changes in tissues, organs or blood indicative of toxicity were observed, even at doses up to 320 mg./kg. In humans, there have been no adverse blood, urine or cardiac changes; liver profiles were negative, and jaundice has not been noted.

without serious side effects or habituation During three and one-half years of clinical study in 1,759 patients,[2-13] Listica has produced no serious side effects. Less than 4% of patients experienced any side effects, and these were invariably minor and transient. Most frequent (38 cases) was mild drowsiness, which disappeared after the first few days of Listica therapy. Habituation, cumulative effects, or withdrawal symptoms have not been noted, even in patients taking Listica as long as two years.

with convenient dosage and availability One Listica tablet, q.i.d., is the recommended dosage. Listica is supplied in bottles of 50 tablets on prescription only, by pharmacies everywhere. Each tablet contains 200 mg. of Hydroxyphenamate, Armour.

References:

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ARMOUR PHARMACEUTICAL COMPANY, KANKAKEE, ILLINOIS
Physicians who prefer generic names prescribe "Hydroxyphenamate, Armour."

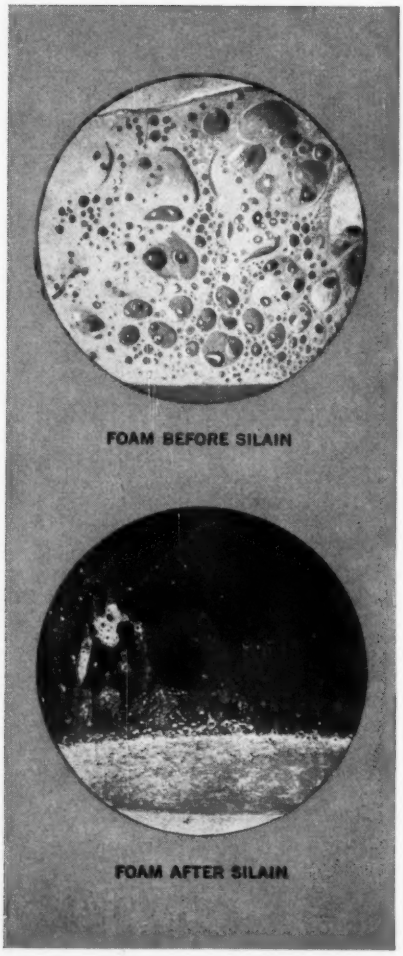
LISTICA—Hydroxyphenamate, Armour. © 1961, A.P. CO. *Stedman's Medical Dictionary

in abdominal distention

Associated with air swallowing, functional indigestion, spastic colitis, diverticulitis, peptic ulcer, postoperative gas.

NEW SILAIN™

The original brand of methylpolysiloxane



a gastrointestinal DEFROTHICANT*

Air swallowing, abnormal peristalsis or "nervous indigestion" accelerates foaming. Foam and froth increase the volume of gastrointestinal contents causing discomfort.

SILAIN *dispels foam and froth*

Even normal peristalsis may produce thick, viscous foam in the presence of gastric mucin and gas forming digestive processes.

SILAIN *reduces increased volume*

By lowering interface cohesion, SILAIN breaks down the gas bubbles reducing the foam to a liquid.

SILAIN *provides fast relief*

Relief occurs promptly when foam is broken—entrapped gas is liberated for normal absorption or eliminated by belching or passing flatus—volume decreases immediately.

SILAIN *is safe*

A single non-toxic compound, SILAIN acts physically with no effect on gastrointestinal motility.

FORMULA: Each tablet contains 50 mg. methylpolysiloxane.

DOSAGE: 1 or 2 tablets after meals or more frequently if necessary.

AVAILABLE: 50 mg. tablets in bottles of 100.

Clinical trial supply on request

*DEFROTHICANT—The property of preventing and eliminating foam.

U. S. Patent No. 2,951,011

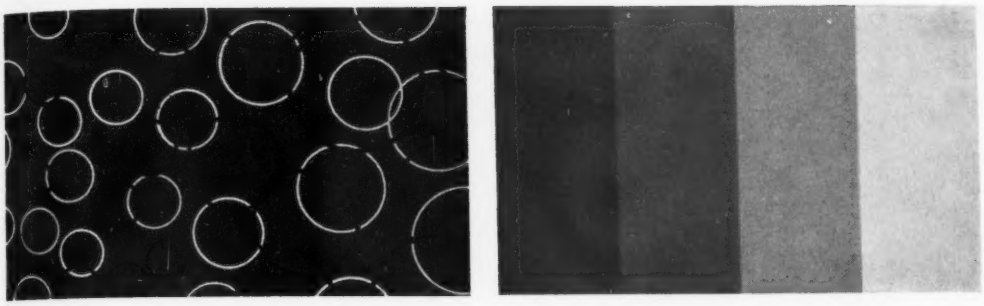
PLOUGH LABORATORIES, INC.

A Subsidiary of Plough, Inc., Memphis, Tennessee

in peptic ulcer, hyperacidity, heartburn

Control Gastric

GAS ACID



TABLETS

NEW SILAIN-GEL T.M.

DEFROTHICANT ANTACID

SILAIN-GEL ***non-fatiguing, fruit-mint taste***

Releases Gas—The unique physical property of SILAIN breaks the frothy bubbles liberating the gas for elimination.

Neutralizes Acid—Specially balanced antacid formulation provides efficient neutralization.

DOSAGE—2 tablets after meals and at bedtime. The safety of Silain-Gel permits administration as often as necessary.

FORMULA—Each tablet contains: methylpolysiloxane 25 mg.; magnesium hydroxide 85 mg.; co-precipitated magnesium carbonate and aluminum hydroxide 282 mg.

REFERENCES

1. Roth, J.L.A. and Bockus, H.L.: Aerophagia—Med. Clin. N. Am. *41*:1673 (Nov.) 1957
2. Alvarez, W.C.. Gas in the Bowel: An Introduction to Gastroenterology; Paul B. Hoeber, Inc. Alvarez, W.C.; Syndrome of Reverse Peristalsis: Ibid
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PLOUGH LABORATORIES, INC.

A Subsidiary of Plough, Inc., Memphis, Tennessee

when G.I. patients double up with pain... double up on symptomatic relief

℞ ENARAX®

(oxyphencyclimine plus ATARAX®)

In peptic ulcer and functional bowel distress
ENARAX provides dual relief of symptoms: it decreases acid flow and spasm . . . **and** relieves tension.

Plus protection against flare-ups
ENARAX works continuously . . . gives dependable 24-hour control, usually with b.i.d. dosage.

Here's how: ENARAX combines oxyphencyclimine, an inherently long-acting anticholinergic (no slip-ups due to coatings or timing devices), plus Atarax,* one of the best tolerated tranquilizers, to decrease tension without increasing gastric secretion. The result: demonstrated success in 87% of cases.[1]

Anticholinergics alone are often not enough. But G. I. complaints like "burning," hyperacidity, pain, spasm and associated tension have one hopeful thing in common: they usually respond to your prescription for ENARAX.

Dosage: The usual dosage is one ENARAX 5 or ENARAX 10 tablet twice daily—preferably in the morning and before retiring. Maintenance dose should be adjusted according to therapeutic response. Use with caution in patients with prostatic hypertrophy and only with ophthalmological supervision in glaucoma.

Supplied: ENARAX 5 (oxyphencyclimine HCl 5 mg., Atarax 25 mg.) and ENARAX 10 (oxyphencyclimine HCl 10 mg., Atarax 25 mg.), bottles of 60.

1. Hock, C. W.: Am. J. Gastroenterol. **34**:293 (Sept.) 1960.

*brand of hydroxyzine

FOR HEMATOPOIETIC STIMULATION WHERE OCCULT BLEEDING IS PRESENT: **HEPTUNA® PLUS** — Balanced Hematinic Formula

ROERIG ℞

New York 17, N.Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being®

from depression to the right frame of mind

continuous, 24-hour cerebral oxygenation for the aging patient. By stimulating respiratory and circulatory function, GERONIAZOL TT* relieves mental confusion, depression, anxiety, and emotional instability—frequent problems in patients after forty—due to presenile changes in the vasculature of the brain. Notable benefit usually is seen within one to three weeks of therapy. It improves appetite, sleep pattern, and outlook—and GERONIAZOL TT* is non-hypertensive, non-excitatory.

Neither a tranquilizer nor a psychic energizer, GERONIAZOL TT* provides a physiologic stimulation of the cerebrum to permit the patient to adjust to his surroundings, become part of life itself again—and *attain the right frame of mind.*

References: 1. Curran, T. R., and Phelps, D. K.: Am. Pract. & Dig. Treat. *11:* 617, 1960. 2. Levy, S.: J.A.M.A. *153:* 1260, 1953. 3. Connolly, R.: W. Va. Med. J. *56:* 263, 1960.

Each TEMPOTROL contains: Pentylenetetrazol, 300 mg.; and Nicotinic Acid, 150 mg.

Indications: Respiratory and circulatory stimulant for the aged and debilitated with symptoms of mental confusion, depression, anxiety or arteriosclerotic psychosis.

Contraindications: None known in recommended dosage.

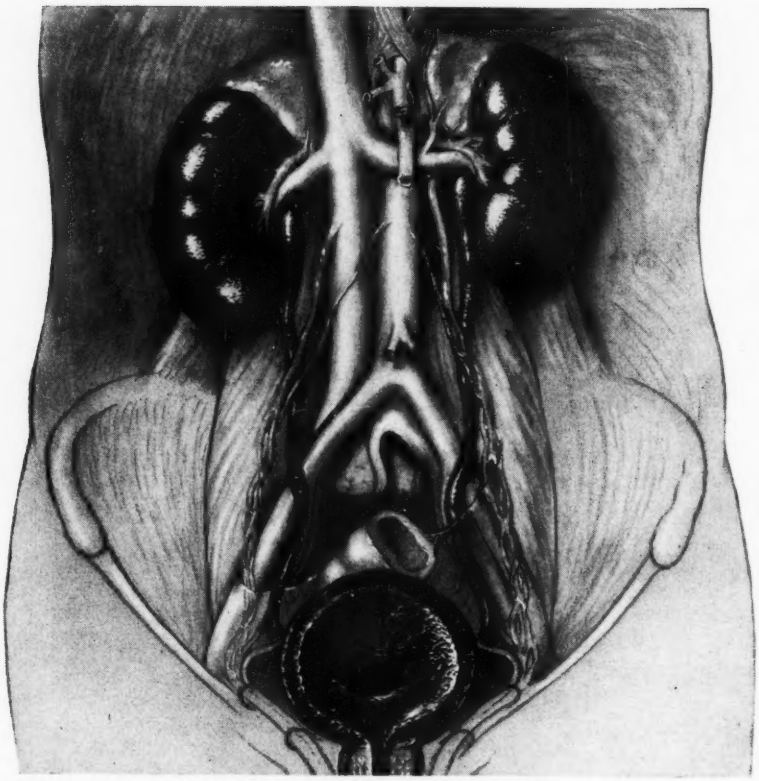
Dosage: One GERONIAZOL TT* tablet, b. i. d.

Supplied: Bottles of 42 tablets (3 weeks' treatment).

GERONIAZOL® TT*

*TEMPOTROL® (Time Controlled Therapy)

PHILIPS ROXANE, INC. Columbus 16, Ohio



Why a triple sulfonamide?

SPECTRUM— that encompasses certain common bacteria not susceptible to antibiotics, such as gram-negative bacteria of the urinary tract.

EFFICACY— in many genito-urinary infections. In upper respiratory infections and genito-urinary infections, active at the foci of infection. May succeed where bacteria are resistant to antibiotics. Rapid bacteriostatic effect.

SAFETY— safer than a single sulfonamide. Independent solubilities of the three sulfonamide components minimize danger of crystalluria. Fewer of the complications of antibiotic therapy such as allergic reactions, diarrhea, gastrointestinal upset, superinfection.

ECONOMY— lower cost to the patient than with most antibiotic prescriptions.

SUSPENSION TABLETS

SULFOSE®

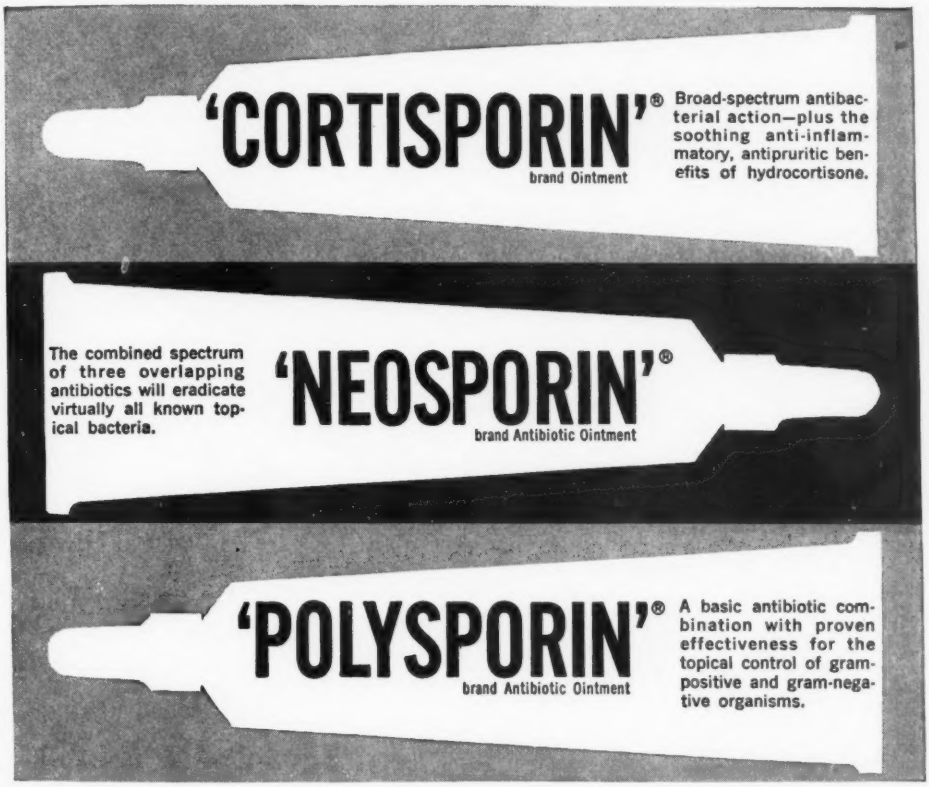
Triple Sulfonamides, Wyeth
(Sulfadiazine, Sulfamerazine, Sulfamethazine)

For further information on limitations, administration, and prescribing of SULFOSE, see descriptive literature or current Direction Circular.

Wyeth® SERVICE TO MEDICINE

Wyeth Laboratories
Philadelphia 1, Pa.

'B. W. & Co.' 'Sporin' Ointments rarely sensitize . . . give decisive bactericidal action for most every topical indication


'CORTISPORIN'®
brand Ointment
Broad-spectrum antibacterial action—plus the soothing anti-inflammatory, antipruritic benefits of hydrocortisone.
The combined spectrum of three overlapping antibiotics will eradicate virtually all known topical bacteria.
'NEOSPORIN'®
brand Antibiotic Ointment
'POLYSPORIN'®
brand Antibiotic Ointment
A basic antibiotic combination with proven effectiveness for the topical control of gram-positive and gram-negative organisms.

Contents per Gm.	'Polysporin'®	'Neosporin'®	'Cortisporin'®
'Aerosporin'® brand Polymyxin B Sulfate	10,000 Units	5,000 Units	5,000 Units
Zinc Bacitracin	500 Units	400 Units	400 Units
Neomycin Sulfate	—	5 mg.	5 mg.
Hydrocortisone	—	—	10 mg.
Supplied:	Tubes of 1 oz., ½ oz. and ⅛ oz. (with ophthalmic tip)	Tubes of 1 oz., ½ oz. and ⅛ oz. (with ophthalmic tip)	Tubes of ½ oz. and ⅛ oz. (with ophthalmic tip)

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, New York

me? use vinegar?

my doctor recommends Massengill Powder!

Patients like Massengill Powder. *Its clean, refreshing fragrance and convenience are acceptable to the most fastidious.*

Massengill Powder offers other sound advantages. Massengill Powder *is buffered to maintain a pH of 3 to 4.5 for 4 to 6 hours in ambulant patients . . . 24 hours in recumbent patients.* Vinegar douches are quickly neutralized.

Massengill Powder has a low surface tension (50 dynes/cm.; vinegar is 72 dynes/cm.). *This lower surface tension means more effective penetration and cleansing of the folds of the vaginal mucosa.*

Massengill Powder is a valuable adjunct in treatment of vaginal infections. Its low pH inhibits proliferation of fungal, protozoan and bacterial pathogens but is favorable to the beneficial Döderlein bacilli.

Patient cooperation is assured when Massengill Powder is recommended. Write for samples and literature.

Formula: Ammonium Alum, Boric Acid, Phenol, Eucalyptol, Berberine Salt, Menthol Isomers, Thymol and Methyl Salicylate.

MASSENGILL® POWDER

THE S. E. MASSENGILL COMPANY

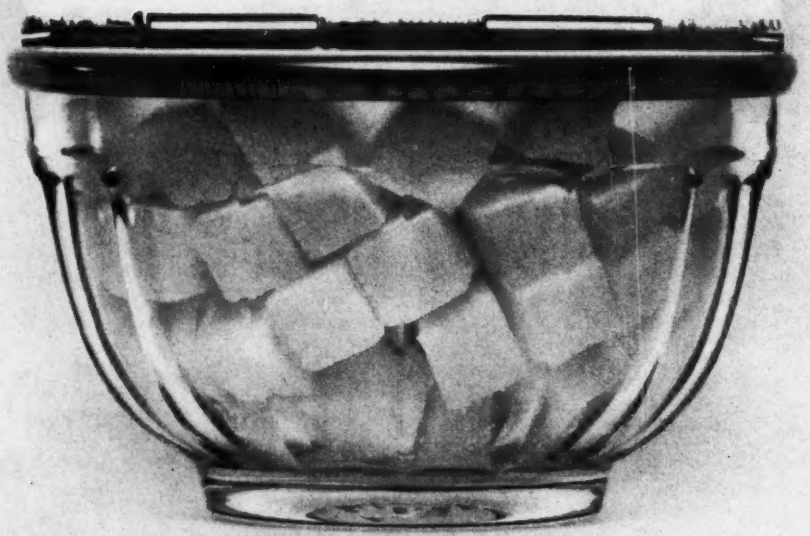
Bristol, Tennessee • New York • Kansas City • San Francisco

AN AMES CLINIQUICK®

CLINICAL BRIEFS FOR MODERN PRACTICE

Quality of diabetic control & Quantitation of urine-sugar

In the diagnosis of diabetes, the urine-sugar test may be little more than a screening adjuvant. But in the everyday management of diabetes, the urine-sugar test is the most practical guide we have.[1] Routine testing, however, should not only detect, but also determine the **quantity** of urine-sugar. Quantitative testing is essential for satisfactory adjustment of diet, exercise and medication. Furthermore, day-to-day control of diabetes is in the patient's hands. Quality of control is thus best assured by the urine-sugar test which permits the most accurate quantitation practicable **by the patient.**



CLINITEST® permits a high degree of practical accuracy and is very convenient.[2] Its clinically standardized sensitivity avoids trace reactions, and a standardized color chart minimizes error or indecision in reading results. CLINITEST distinguishes clearly the critical ¼%, ½%, ¾%, 1% and 2% urine-sugars. It is the only simple test that can show if the urine-sugar is over 2%.[3] Your nurse or technician will appreciate these advantages; your patient on oral hypoglycemic therapy will find them helpful. Furthermore, CLINITEST may be a vital adjunct in the management of the diabetic child or the adult with severe diabetes.

(1) Danowski, T. S.: Diabetes Mellitus, Baltimore, Williams & Wilkins, 1957, p. 239. (2) McCune, W. G.: M. Clin. North America 44:1479, 1960. (3) Ackerman, R. F., et al.: Diabetes 7:398, 1958.

FOR PRACTICAL ACCURACY OF URINE-SUGAR QUANTITATION

COLOR-CALIBRATED

CLINITEST®

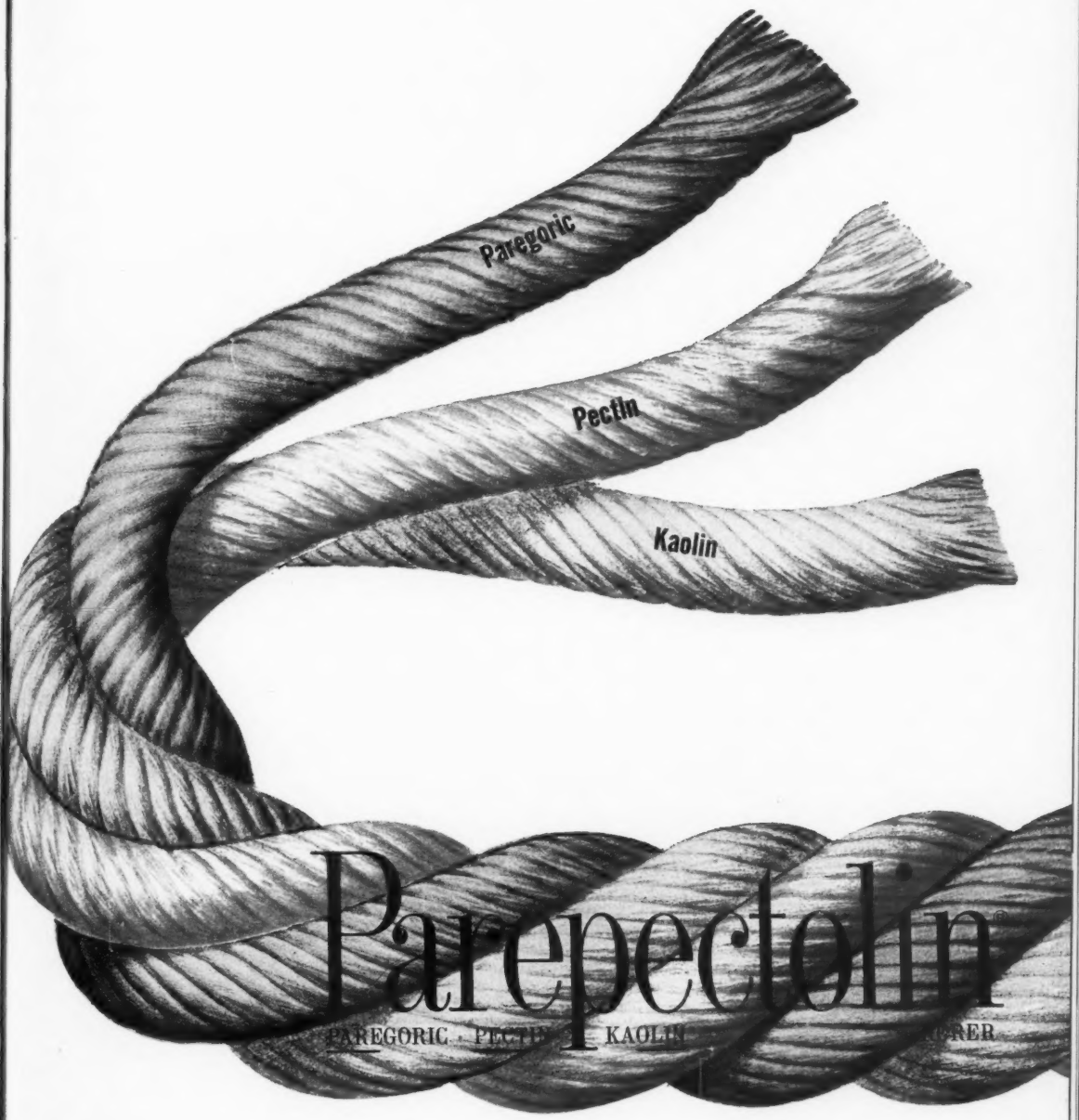
BRAND Reagent Tablets

Standardized urine-sugar test...with **GRAPHIC ANALYSIS RECORD**

A line connecting successive urine-sugar readings reveals at a glance how well diabetics are cooperating. Each CLINITEST Set and tablet refill contains this physician-patient aid. 01861

AMES COMPANY, INC Elkhart, Indiana

CONTROL DIARRHEA... the traditional and time-tested triad of effective and safe agents



Pleasant taste *plus* predictable, prompt response in diarrhea

Parepectolin combines paregoric, pectin, kaolin in *a balanced, stable colloidal suspension,* with a smooth, creamy consistency and a pleasant, mildly aromatic flavor. Parepectolin is compatible with antibiotics, and retains its uniform consistency and its good flavor.

Parepectolin; each fluid ounce—Paregoric (equivalent) 1.0 dram, Pectin 2.5 gr., Kaolin (specially purified) 85 gr. Bottles of 4 and 8 fluid ounces

RORER

WILLIAM H. RORER, INC. PHILADELPHIA, PENNSYLVANIA

AVAILABLE NOW

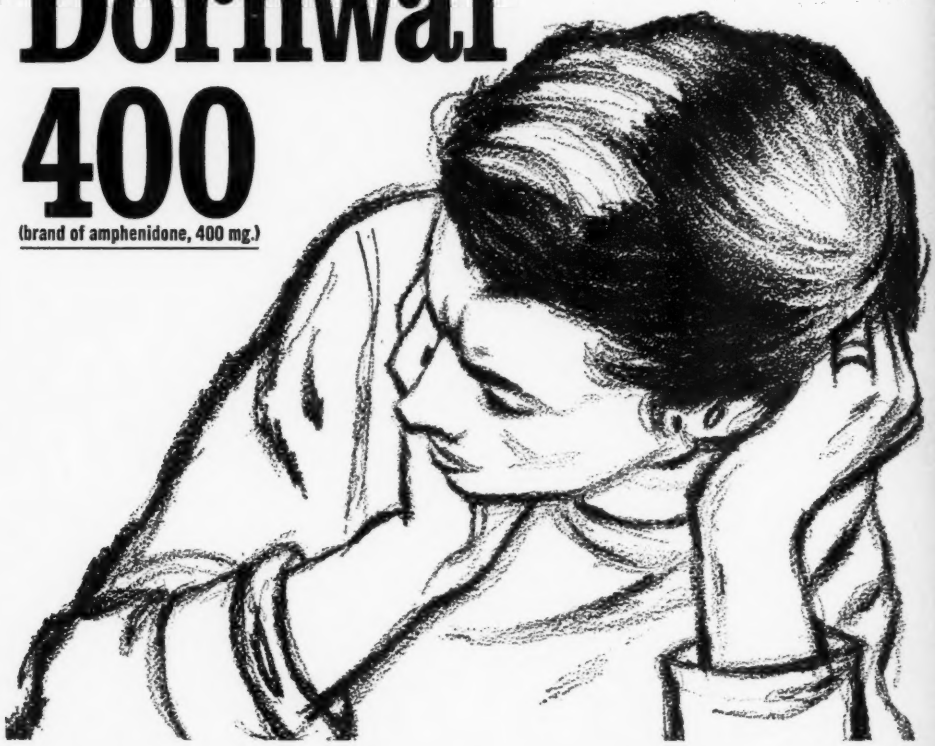
INCREASED POTENCY
GREATER ECONOMY

with

Dornwal®

400

(brand of amphenidone, 400 mg.)



impressively effective against tension headache*

Dornwal 400 relaxes the musculature of the head and neck involved in tension headache and by doing so breaks the vicious cycle between psychological tension and muscular tension. Dornwal 400 also relieves anxiety and tension states quickly and effectively, usually without sedation or drowsiness. It is particularly suited to the active patient because it is relatively free from side effects such as depression and depersonalization. Some patients are relieved of their symptoms in as little as half an hour.

Dornwal 200 (amphenidone, 200 mg.), for similar conditions where lower dosage levels are adequate. Dornwal 100 (amphenidone, 100 mg.) is effective in the treatment of emotionally disturbed children.

Supplied: Dornwal 400—400 mg. green scored tablets. Dornwal 200—200 mg. yellow scored tablets. Dornwal 100 (Pediatric)—100 mg. pink tablets. Bottles of 100 and 500.

Maltbie

Maltbie Laboratories Division

Wallace & Tiernan Inc., Belleville 9, N. J.

*Dixon, H. H.; Dickel, H. A., and Dixon, H. H., Jr.: "Clinical and Electromyographic Appraisal of Aminophenylpyridone," Northwest Med. 60:277 (March) 1961.

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Increasingly,
the
trend is to

Terramycin

OXYTETRACYCLINE WITH GLUCOSAMINE

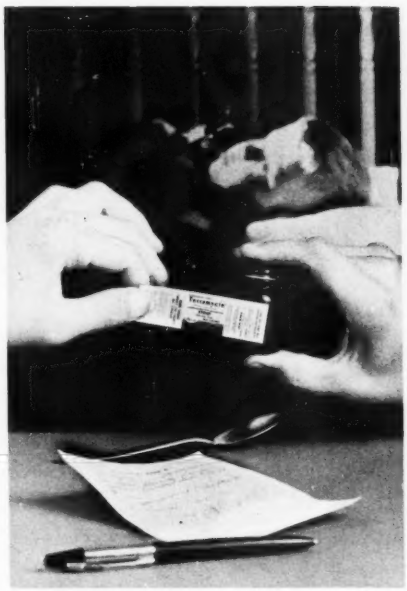
confirmed dependability in otitis media is just one reason why

*New evidence** demonstrates the effectiveness of Terramycin in *otitis media* . . . another reason for the trend to Terramycin.

In a series of 41 cases of otitis media, Terramycin not only "was often successful where other antibiotics had failed," but also showed that "it is extremely well tolerated"; oral dosage for infants was 250 to 375 mg. daily, for children, 500 mg. to 1 Gm. In many instances, oral therapy was preceded by intramuscular injection of Terramycin.

The authors concluded that "there is good reason to consider it [Terramycin] one of the most effective agents for treatment of infection of the upper respiratory tract."

These findings confirm the continuing vitality and broad-spectrum dependability of Terramycin, as reported through more than a decade of extensive clinical use.



In brief

The dependability of Terramycin in daily practice is based on its broad range of antimicrobial effectiveness, excellent toleration, and low order of toxicity. As with other broad-spectrum antibiotics, overgrowth of nonsusceptible organisms may develop. If this occurs, discontinue the medication and institute appropriate specific therapy as indicated by susceptibility testing. Glossitis and allergic reactions are rare. Aluminum hydroxide gel may decrease antibiotic absorption and is contraindicated.

More detailed professional information available on request.

another reason why the trend is to Terramycin—*versatility of dosage form:*

TERRAMYCIN Capsules—
250 mg. and 125 mg. per capsule—for convenient initial or maintenance therapy in adults and older children

TERRAMYCIN Intramuscular Solution—
50 mg./cc. in 10 cc. vials; 100 mg. and 250 mg. in 2 cc. ampules—preconstituted, ready to use where intramuscular therapy is indicated

Terramycin®

OXYTETRACYCLINE WITH GLUCOSAMINE

SYRUP PEDIATRIC DROPS

125 mg. per tsp. and 5 mg. per drop (100 mg./cc.), respectively

deliciously fruit-flavored aqueous dosage forms—conveniently preconstituted

Science for the world's well-being® Pfizer

PFIZER LABORATORIES Division, Chas. Pfizer & Co., Inc.
New York 17, N. Y.

*Jacques, A. A., and Fuchs, V. H.: J. Louisiana M. Soc. 113:200, May, 1961.

New! For pain, distention and distress due to gastrointestinal gas!

Bloating, belching, borborygmus or flatulence—whatever the symptoms of gastrointestinal gas, Phazyme provides uniquely effective relief. Phazyme is the first comprehensive treatment for gastrointestinal gas that combines **both** digestive enzymes **and** gas-releasing agents—dual action that provides far better results than either agent alone. **Digestive enzymes** minimize gas formation resulting from digestive disorders or food intolerance. The gas-releasing agent, **specially activated dimethyl polysiloxane**, breaks down gas-enveloping membranes—prevents gas entrapment. A two-phase tablet, Phazyme releases these active components in the environments best suited to their actions—stomach or small intestine.

Phazyme is ideal medication for relieving gas distress in patients on the currently popular 900-calories-a-day diet. It is also recommended as routine therapy for cardiac patients to prevent gas from aggravating, complicating or simulating angina.

DOSAGE: One tablet with meals and upon retiring, or as required. SUPPLIED: As two-phase release, pink tablets, in bottles of 50 and 100.

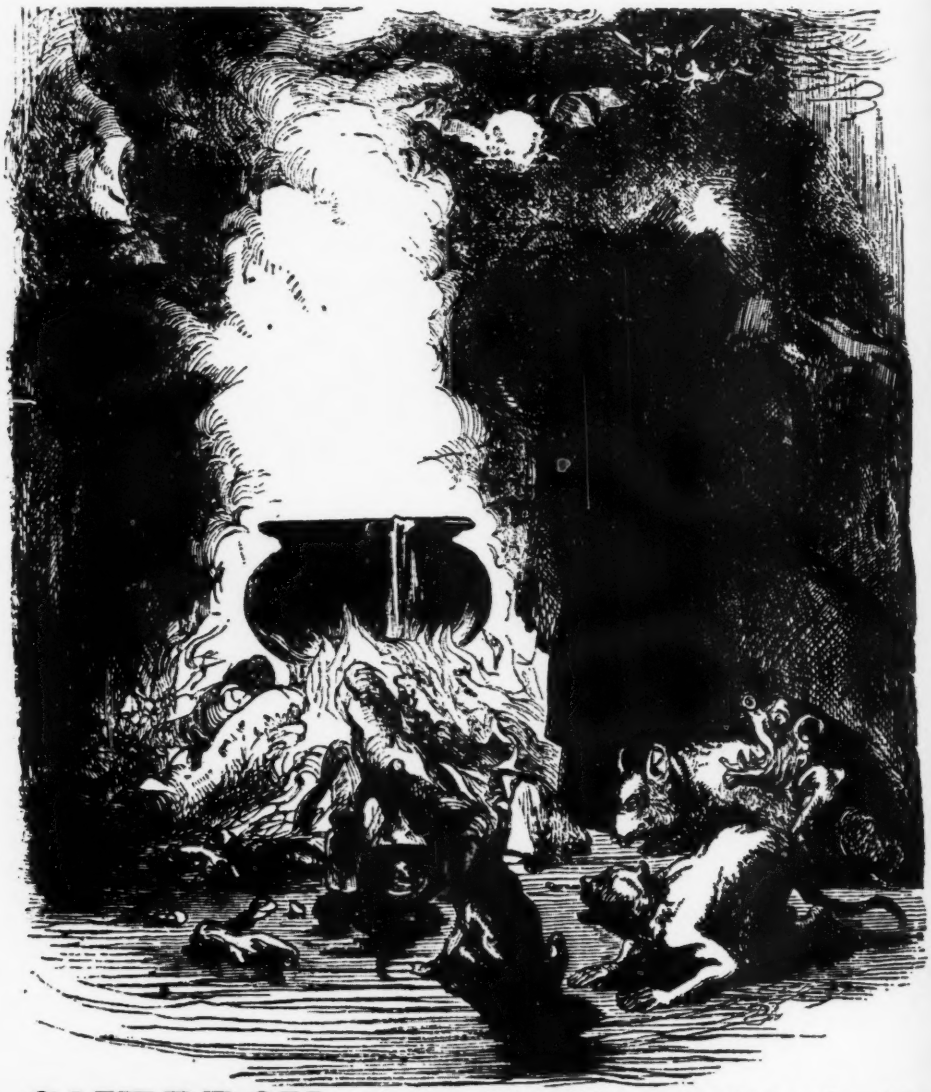
REED & CARNRICK / Kenilworth, New Jersey R&C

minimizes gas formation • prevents gas entrapment

PHAZYME™ TABLETS

When anxiety adds to the gas problem—

Phazyme with Phenobarbital The Phazyme formula with ¼ gr. phenobarbital. Supplied in bottles of 50. Phenobarbital may be habit forming.



CAULDRON BUBBLE GASTRIC TROUBLE

Give immediate relief from heartburn and gastric distress with Al-Caroid. The fine-particle dispersion of balanced antacids in Al-Caroid quickly neutralizes excess gastric acid. The enzyme Caroid added to the Al-Caroid formula prevents interruption of protein digestion. When antacids raise the pH of stomach contents pepsin is inactivated, but the enzyme Caroid continues protein digestion in alkaline or acid media.

AL-CAROID®
antacid powder or tablets

American Ferment Division • Breon Laboratories Inc., New York 18, New York

during pregnancy...
throughout lactation

Natabec®
Kapseals®

prenatal vitamin-mineral formula

Prescribed as a prenatal supplement, NATABEC provides 10 vitamins with calcium and iron plus intrinsic factor concentrate and rutin. These easy-to-swallow Kapseals compensate for the increased demands of pregnancy and lactation...help to promote better health for both mother and child. Each NATABEC Kapseal contains: Calcium carbonate—600 mg.; Ferrous sulfate—150 mg.; Vitamin A (1.2 mg.)—4000 units; Vitamin D (10 mcg.)—400 units; Vitamin B_1 (thiamine) mononitrate—3 mg.; Vitamin B_2 (riboflavin)—2 mg.; Vitamin B_{12} (crystalline)—2 mcg.; Folic acid—0.25 mg.; Synkamin® (as the hydrochloride)—0.5 mg.; Rutin—10 mg.; Nicotinamide (niacinamide)—10 mg.; Vitamin B_6 (pyridoxine hydrochloride)—3 mg.; Vitamin C (ascorbic acid)—50 mg.; Intrinsic factor concentrate—5 mg. *Dosage:* One Kapseal daily or as directed by the physician. *Supplied:* NATABEC Kapseals are available in bottles of 100 and 1,000. 59161

PARKE-DAVIS

PARKE, DAVIS & COMPANY, Detroit 32, Michigan

"my mom took Natabec... so we're both doing fine"

Anem

LIVER,
B-COMPLEX,
IRON
of course

but more!...

SAFE AMOUNTS OF COBALT
AND EXTRA VITAMIN B_{12}

as in **Li-Betaron** ELIXIR

... because Cobalt is the nucleus of the B_{12} molecule — must be present for intestinal bacterial flora to produce B_{12} — is a proven effective catalyst for increasing Hb content and formation of erythrocytes. And, Cobalt in the recommended Li-Betaron dosage is safe, even for infants.

... because Li-Betaron provides immediately-usable B_{12} until normal intestinal synthesis can be stimulated by Cobalt.

DOSAGE

ADULTS — 1 tablespoonful twice daily after meals.
6 to 12 years — 1 or 2 teaspoonfuls twice daily after meals.
1 to 6 years — ½ to 1 teaspoonful twice daily after meals.
INFANTS — 10 to 20 drops (5 to 10 minims) in milk.

SUPPLIED — In pint and gallon bottles.

EACH 30cc CONTAINS

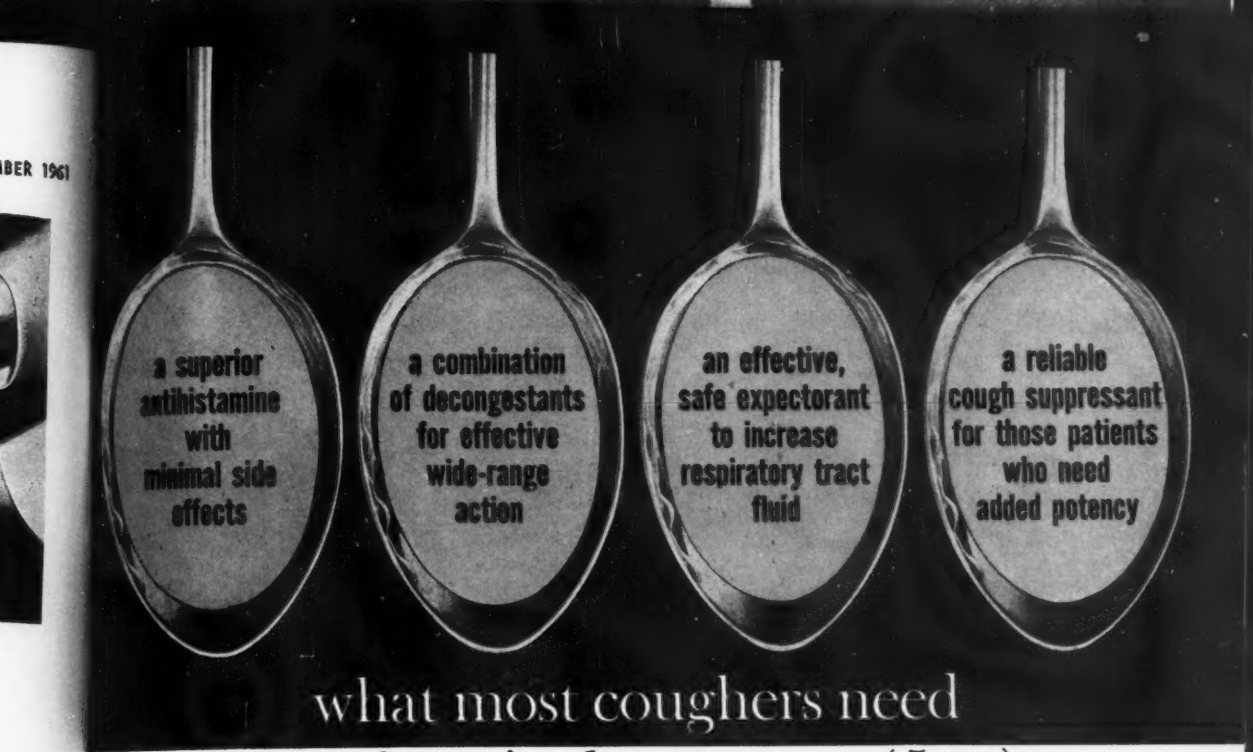
Vitamin B_{12} Crystalline	25 mcg.
Elemental Cobalt (as Cobalt Chloride)	1.5 mg.
Liver Concentrate	1 Gm.
Ferric Ammonium Citrate (10 MDR) (Iron 100 mg.)	572 mg.
Panthenol	5 mg.
Thiamine HCl (18 MDR)	18 mg.
Riboflavin (3 MDR)	6 mg.
Nicotinamide	60 mg.
Pyridoxine HCl	2 mg.

In pernicious anemia, Li-Betaron Elixir is recommended only as a supplement to parenteral use of Liver Injection USP, or equivalent.

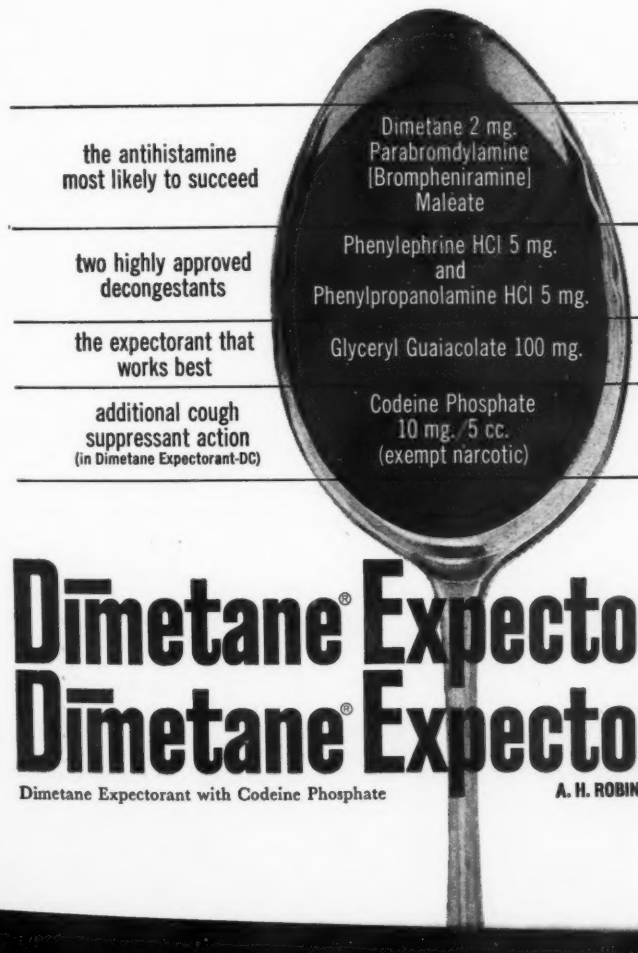
THE WARREN-TEED PRODUCTS COMPANY
COLUMBUS 15, OHIO

Dallas Chattanooga Los Angeles Portland

WARREN-TEED PHARMACEUTICALS


a superior antihistamine with minimal side effects
a combination of decongestants for effective wide-range action
an effective, safe expectorant to increase respiratory tract fluid
a reliable cough suppressant for those patients who need added potency

what most coughers need now in a single teaspoon (5 cc.)


the antihistamine most likely to succeed
Dimetane 2 mg. Parabromdylamine [Brompheniramine] Maleate
two highly approved decongestants
Phenylephrine HCl 5 mg. and Phenylpropanolamine HCl 5 mg.
the expectorant that works best
Glyceryl Guaiacolate 100 mg.
additional cough suppressant action (in Dimetane Expectorant-DC)
Codeine Phosphate 10 mg./5 cc. (exempt narcotic)

Dimetane® Expectorant
Dimetane® Expectorant-DC

Dimetane Expectorant with Codeine Phosphate

A. H. ROBINS CO., INC., RICHMOND 20, VIRGINIA

ASTHMA RELIEF *in seconds*

MEDIHALER®

the most effective anti-asthmatics...

administered in the most effective manner...

simplest and most convenient for the patient...

Available with either of the two outstanding bronchodilators

MEDIHALER-ISO®

Isoproterenol sulfate, 2.0 mg. per cc., suspended in inert, nontoxic aerosol vehicle. Contains no alcohol. Each automatically measured dose contains 0.075 mg. isoproterenol.

MEDIHALER-EPI®

Epinephrine bitartrate, 7.0 mg. per cc., suspended in inert, nontoxic aerosol vehicle. Contains no alcohol. Each automatically measured dose contains 0.15 mg. epinephrine.

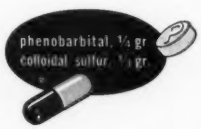
Usual precautions for administration of isoproterenol and epinephrine should be observed.

Riker Northridge, California

Condition not acute
Diagnosis not obvious ?

Solfoton®

Solfoton will relieve the symptoms due to emotional stress and assist in creating empathy with the patient if prescribed during the diagnostic study. Solfoton will lower the emotional titer, and improve the mental climate for health.



DOSAGE: One tablet or capsule after meals and at bedtime.

Complete information sent upon request.

WM. P. POYTHRESS & COMPANY, INC., RICHMOND, VIRGINIA
Manufacturers of ethical pharmaceuticals since 1856.

Cremomycin® provides rapid relief of virtually all diarrheas

NEOMYCIN—actively bactericidal against a wide range of gram-negative intestinal pathogens, but relatively ineffective against certain diarrhea-causing organisms.

SULFASUXIDINE® succinylsulfathiazole—an ideal adjunct to neomycin because it is highly effective against Clostridia and certain other neomycin-resistant organisms.

KAOLIN AND PECTIN—coat and soothe the inflamed mucosa, adsorb toxins, help provide rapid symptomatic relief.

Additional information on CREMOMYCIN is available to physicians on request.

MSD MERCK SHARP & DOHME, DIVISION OF MERCK & CO., INC., WEST POINT, PA.

CREMOMYCIN AND SULFASUXIDINE ARE TRADEMARKS OF MERCK & CO., INC.

With its combination of 5 proven therapeutic agents, BRONKOTABS dilates the bronchioles... thins and helps expel thick mucus... combats local edema... offers mild sedation... and treats the allergic component. Gets right to the root of asthmatic distress with minimal side effects, and none of those associated with steroids.

In a study of 40 patients with bronchial asthma, 24 persons (60%) reported BRONKOTABS brought good relief from asthmatic symptoms – ease of expectoration, reduction of bronchospasm and increased vital capacity. Only seven patients failed to respond at all. "The combination of drugs used [in Bronkotabs] gave greater relief in these patients than the conventionally used tablet [ephedrine, theophylline, phenobarbital]..."[1]

In another study, 79.7% of 64 asthma patients showed good to excellent response to BRONKOTABS therapy.[2]

Each tablet contains; theophylline 100 mg.; ephedrine sulfate 24 mg.; phenobarbital 8 mg. (warning: may be habit forming); thenyldiamine HCl 10 mg.; and glyceryl guaiacolate 100 mg. Supplied: bottles of 100 white scored tablets. Usual precautions associated with sympathomimetic amines should be observed.

References: 1. Spielman, A. D.: Evaluation of a Combination Tablet of Theophylline, Ephedrine Sulphate, Phenobarbital, Thenyldiamine and Glyceryl Guaiacolate in the Treatment of Chronic Asthma, Ann. Allergy 18:281, 1960. 2. Waldbott, G.: Bronkotabs – a New Antiasthmatic Preparation (Preliminary Report), Int. Arch. Allergy 17:116, 1960.

For full information on Breon's five antiasthmatics, see pp. 538-539 of the 1961 PHYSICIANS' DESK REFERENCE plus the 2nd, 3rd, or 4th quarterly supplement.

BRONKOTABS®

CLEARS and DILATES the bronchial tree with MINIMAL SIDE EFFECTS[1,2]

a full line of antiasthmatics designed to meet every patient's need

BREON Rx Products Division, Breon Laboratories Inc., New York 18, N. Y.

HISTA-VADRIN

when antihistamines alone are not enough

HISTA-VADRIN, an upper respiratory decongestant, is designed for the oral relief of congestion and edema of the upper respiratory passages. The ANTIHISTAMINIC drugs methapyriline and chlor-pheniramine are noted for their ability to prevent vasodilatation and inflammatory edema caused by the release of histamine.

VASOCONSTRICTORS, phenylpropanolamine and phenylephrine oppose mucosal edema by constricting blood vessels which have been dilated by histamine and other factors involved in inflammation. These vasoconstrictors are not as likely to cause excitement or wakefulness as ephedrine or methamphetamine (1).

Indications: For the relief of hay fever, vasomotor rhinitis, and symptoms resulting from upper respiratory infections. Hista-vadrin can afford relief also in other allergic conditions such as urticaria and angioedema.

Each scored Hista-vadrin tablet contains:

Phenylpropanolamine Hydrochloride	40 mg.
Chlor-Pheniramine Maleate	4 mg.
Methapyriline Hydrochloride	40 mg.
Phenylephrine Hydrochloride	5 mg.

Dosage: Adult Dose, 1 tablet every six hours or in accordance with therapeutic response.

Supplied: Slow release scored tablets designed to disintegrate in 2 to 3 hours.

Reference available on request.

Samples and professional literature on request.

HISTA-VADRIN is another "established need" product

in our 61st year .. FTP **First Texas *Pharmaceuticals, Inc.***

DALLAS, TEXAS • SINCE 1901

WHY GANTRISIN IS PREFERRED

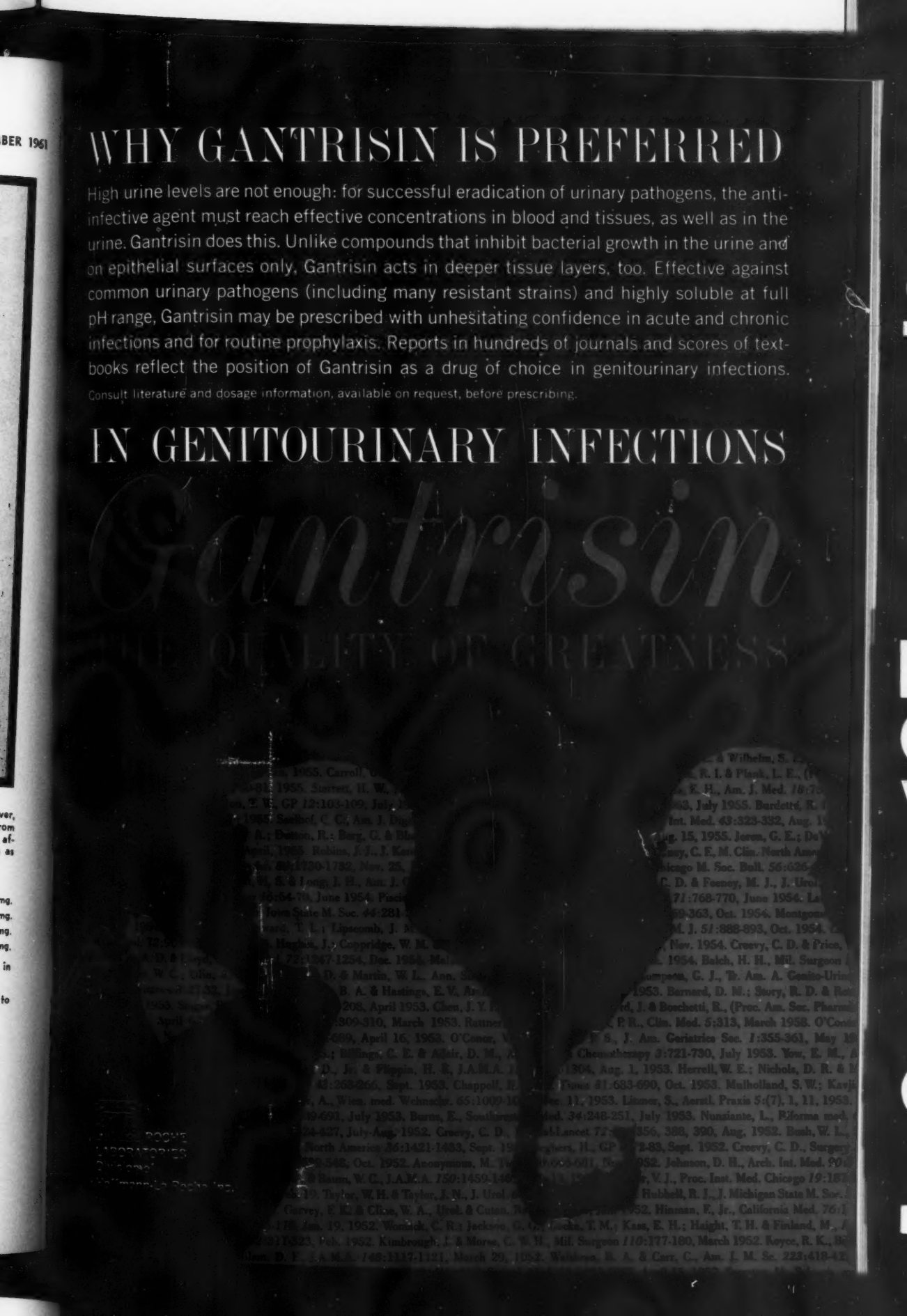
High urine levels are not enough: for successful eradication of urinary pathogens, the anti-infective agent must reach effective concentrations in blood and tissues, as well as in the urine. Gantrisin does this. Unlike compounds that inhibit bacterial growth in the urine and on epithelial surfaces only, Gantrisin acts in deeper tissue layers, too. Effective against common urinary pathogens (including many resistant strains) and highly soluble at full pH range, Gantrisin may be prescribed with unhesitating confidence in acute and chronic infections and for routine prophylaxis. Reports in hundreds of journals and scores of textbooks reflect the position of Gantrisin as a drug of choice in genitourinary infections.

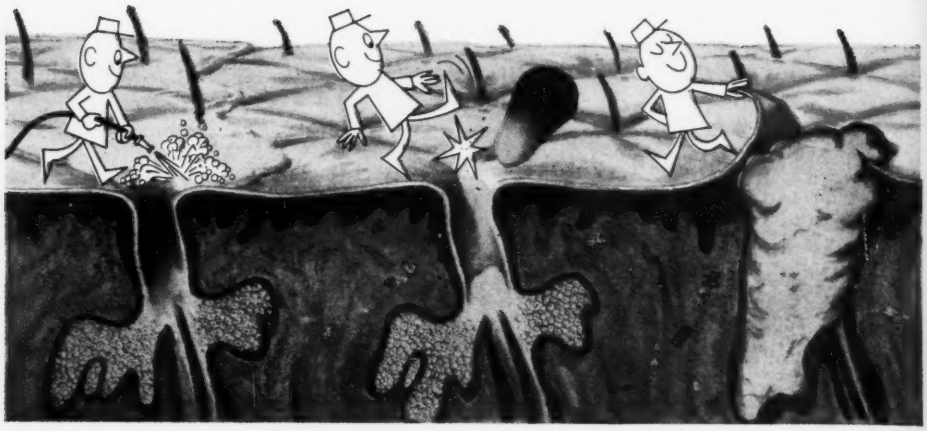
Consult literature and dosage information, available on request, before prescribing.

IN GENITOURINARY INFECTIONS

Gantrisin

THE QUALITY OF GREATNESS





Fostex® treats pimples·blackheads·acne while they wash

degreases the skin
helps remove blackheads
dries and peels the skin

Patients like Fostex because it's so easy to use. Instead of using soap, they simply wash acne skin with Fostex Cream or Fostex Cake 2 to 4 times daily.

Fostex contains: Sebulytic® base (unique, penetrating, surface-active combination of soapless cleansers and wetting agents*) with remarkable antiseborrheic, keratolytic and antibacterial actions . . . enhanced by micropulverized sulfur 2%, salicylic acid 2% and hexachlorophene 1%.

*sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate and sodium dioctyl sulfosuccinate.

Fostex Cream and Fostex Cake are interchangeable for therapeutic washing of the skin. Fostex Cream is approximately twice as drying as Fostex Cake. Supplied: Fostex Cake—bar form. Fostex Cream—4.5 oz. jars. Also used as a therapeutic shampoo in dandruff and oily scalp.

And . . . since continuous 24-hour drying and peeling of acne skin is essential, FOSTRIL (a new, flesh-tinted drying lotion) should be used once or twice daily in addition to Fostex therapeutic washings. Fostril® contains Liposec® (polyoxyethylene lauryl ether), a new, surface-active drying agent used for the first time in acne treatment. This agent, with 2% micropulverized sulfur and a zinc oxide, talc and bentonite base, provides Fostril with excellent drying properties. Fostril also contains 1% hexachlorophene.

Available: Fostril, 1½ oz. tubes. Fostril-HC (¼% hydrocortisone) 25 gm. tubes.

WESTWOOD PHARMACEUTICALS • Buffalo 13, New York

Butazolidin®

brand of phenylbutazone

Geigy

in arthritis and allied disorders

Proved by a decade of experience

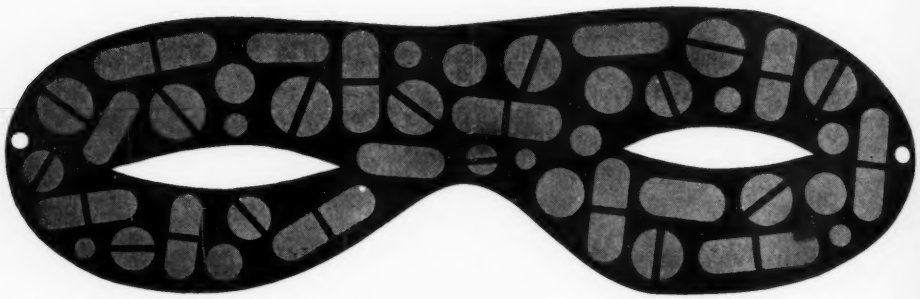
Ten years of world-wide experience... almost 2000 published reports... have progressively entrenched Butazolidin as the leading nonhormonal antiarthritic agent.

In virtually all forms of arthritic disorder, Butazolidin affords prompt symptomatic and objective improvement without development of tolerance... without danger of hypercortisonism.

Butazolidin®, brand of phenylbutazone, tablets of 100 mg.; Butazolidin® alka capsules containing Butazolidin, 100 mg.; dried aluminum hydroxide gel, 100 mg.; magnesium trisilicate, 150 mg.; homatropine methylbromide, 1.25 mg.

Geigy Pharmaceuticals
Division of Geigy Chemical Corporation
Ardsley, New York

BU 564-61



drugs anonymous

One of the several hastily conceived and potentially dangerous suggestions for reducing drug costs is generic-name prescribing. The proponents of generic-name prescribing claim that it will lower drug costs significantly and—through supervision by the Federal Government—provide quality equivalent to that of trademarked drugs. We maintain that these claims are false. Here are some authoritative answers to the principal questions posed by generic-name prescribing.

How much money would be saved if all prescriptions were written for generic-name drugs?

"The [Rhode Island] Division of Public Assistance examined 10,000 drug prescriptions for welfare recipients for the purpose of determining the actual savings . . . of generic versus trade-name drugs. The drugs had cost $28,000. Substituting generic drugs whenever possible would have provided a saving of less than 5 per cent. Syracuse has made a similar study of drug costs with comparable results."

Rhode Island Medical Journal,
January, 1961

Are the savings worth the risk of sacrificing quality?

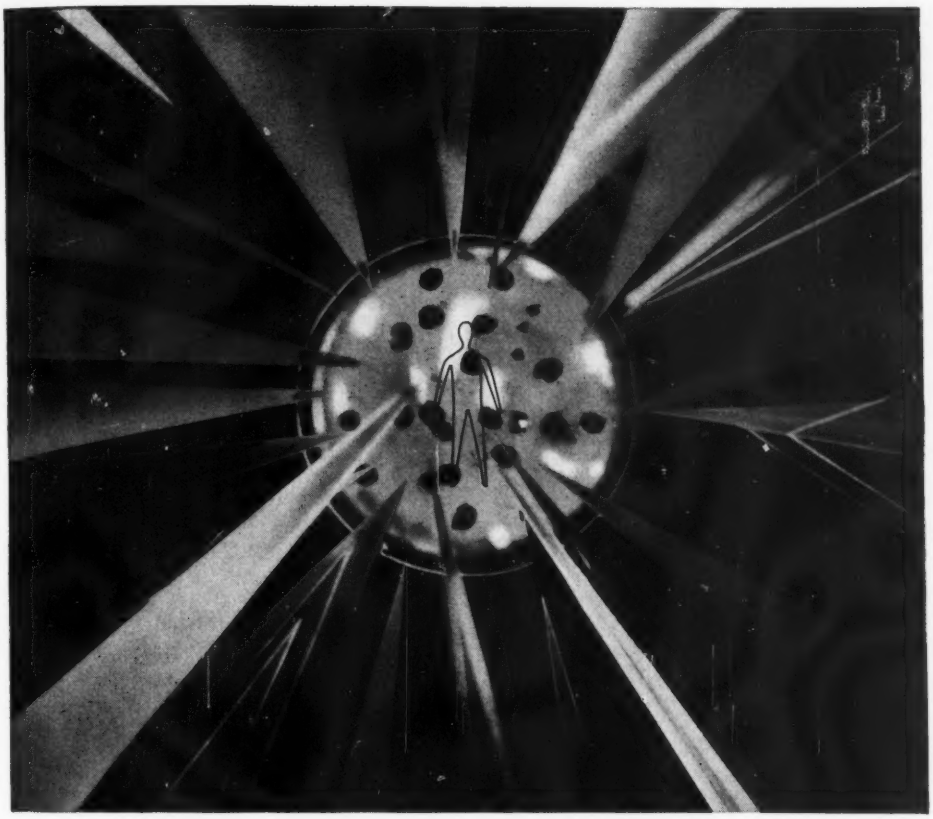
". . . it is unsafe [to prescribe generically] because there is not sufficient policing of our standards. . . ."

Lloyd C. Miller, Ph. D.
Director of Revision of the U.S.P.

"The naive belief that, if a product was not good, the FDA would prohibit its sale is just not realistic. . . . it is completely impossible for the FDA to check every batch of every product of every manufacturer. . . . Hence the integrity and reputation of the manufacturer assume unusual significance where drugs and health products are concerned."

Albert H. Holland, M.D.
formerly Medical Director of the
Food and Drug Administration

Smith Kline & French Laboratories, Philadelphia SK&F



Why do we say Mysteclin-F is decisive in infection?

because... it contains phosphate-potentiated tetracycline
for prompt, dependable broad spectrum antibacterial action.

because... it contains Fungizone, the antifungal antibiotic,
to prevent monilial overgrowth in the gastrointestinal tract.

Mysteclin-F resolves many respiratory, genitourinary and gastrointestinal infections—as well as such other conditions as cellulitis, bacterial endocarditis, furunculosis, otitis media, peritonitis, and septicemia. It combats a truly wide range of pathogenic organisms: gram-positive and gram-negative bacteria, spirochetes, rickettsias, viruses of the psittacosis-lymphogranuloma-trachoma group.

Available as: Mysteclin-F Capsules (250 mg./50 mg.) Mysteclin-F Half Strength Capsules (125 mg./25 mg.) Mysteclin-F for Syrup (125 mg./25 mg. per 5 cc.) Mysteclin-F for Aqueous Drops (100 mg./20 mg. per cc.)
'Mysteclin'®, 'Sumycin'® and 'Fungizone'® are Squibb trademarks.

Mysteclin-F

For full information, see your Squibb Product Reference or Product Brief.

SQUIBB *Squibb Quality— the Priceless Ingredient*

Squibb Phosphate-Potentiated Tetracycline (SUMYCIN) *plus* Amphotericin B (FUNGIZONE)

uterine relaxation
with no side effects

Lutrexin®

TABLETS

(H.W. & D. brand of lututrin)

IN PREMATURE LABOR
THREATENED AND HABITUAL ABORTION
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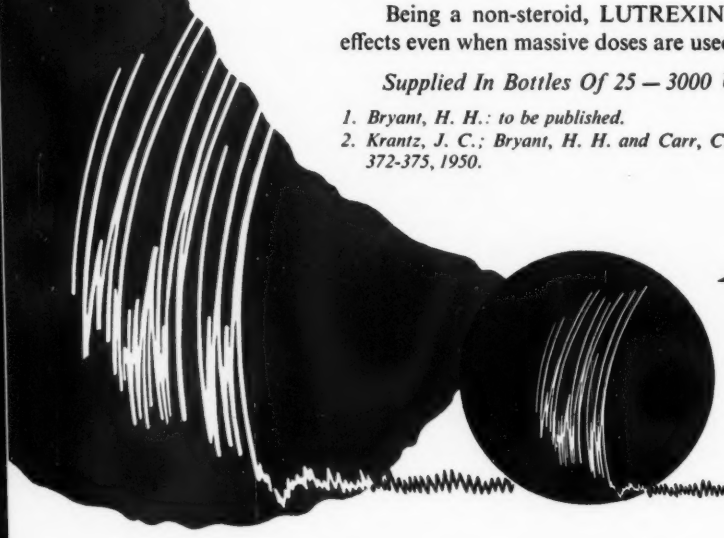
1. Bryant, H. H.: to be published.
2. Krantz, J. C.; Bryant, H. H. and Carr, C. J.; Surg., Gyn. & Obst., 90: 372-375, 1950.



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Chronic Dependency in Emotional Illness*

E. L. CAVENY, M.D.,† *Birmingham, Ala.*

The need for fulfillment of dependency is basic in normal emotional development. Its lack may be reflected in later life in either the psychologic sphere or in that of the psychosomatic.

DEPENDENCY, the subject of this paper, forms a part of the psychologic makeup of every individual. This dependency is a distinct necessity to childhood and is continued on into later years in varying degrees and in methods of expression. The influence of the presence of dependency varies greatly; it may be a source of either pleasure or displeasure, health or illness. Even though dependency furnishes the basis for a large percentage of emotional and behavioral disturbances in adult life, in moderation it is a blessing in disguise. It is a source of comfort and contentment, a necessary adjunct to good interpersonal relationships and emotional health; as such it is certainly not a problem. The normal adult person is capable of, and on occasions does regress to varying levels of carefree childhood, as well as he is capable of, and does suppress the urges to do so in situations when it is not appropriate to adult demands. The retained dependency needs in the adult, in this manner, experience fulfillment. Such normally controlled retained dependency is an accompaniment of good health and relaxation common to the independence of adulthood.

One of the outstanding phenomena in the development of human personality is involved in the subject under consideration. The child progressively matures from clinging dependency on the parents to the adult person capable of caring for himself, only to enter an area of continual conflict against the tendency of that personality to later regress from the more mature patterns to earlier, dependent, immature ones. Probably one of the basic unresolved conflicts in neurotic disorders arises from the long continued dependency of the human young. When the time comes for adult behavior of independence and self-reliance, the individual begins to doubt his own strength and values. Possibly, it is on this level that the dependency processes remaining within an individual have a basic and fundamental importance in practically all illnesses.

Chronic dependency, as with other psycologic factors, depends on its manner and degree of utilization as to whether it is an asset or a disturbance to adult adjustment. The child's dependence and motivations are never completely outgrown; what is important is how much remains quantitatively and its influence in shaping the person's behavior in his adult environment. Obviously there are times when it is unwise to resort to chronic dependency, and to do so is a distinct immature desire to retreat from adult responsibility. The chronically dependent person who is having difficulty in environmental adjustment is not unlike any other emotionally ill person. There is one basic personality defect common to all, that of emotional immaturity. The difference in symptomatology depends upon the life experiences of the respective in-

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†From the Department of Psychiatry, Medical College of Alabama, and The Frank Kay Clinic, Birmingham, Ala.

dividual. While other emotionally ill people regress to varying levels of dependency in the course of their illness, the chronically dependent individual has failed to ever reach an adequate level of emotional maturity. When this type of individual becomes emotionally ill, it comes about through encountering varying environmental stresses to which his previous learning experience has been lacking and wherein he finds his persistent dependency needs going unfulfilled.

When the patient comes to the doctor, he is seeking help for discomfort, the nature of which he, the patient, feels incapable of caring for. Considering that there is always in the adult some of the child's dependence emotionally, the accompanying attitude in some ways resembles the helplessness of the child, and once again the patient is dependent on others, only this time the assistance is forthcoming from a substitute for the parent in the form of the physician. In his approaching the doctor, he does so with faith and hope, as an individual might turn to his broker or lawyer. It is then primarily through the ability of the doctor that a good patient-doctor relationship is developed, from which confidence is acquired by both patient and physician; it is with this relationship adjunct that treatment will more probably come to the hoped for successful end.

In all phases of medical practice there are encountered varying psychiatric situations requiring prompt recognition and appraisal on the part of the attending physician. The more common and probably most frequently encountered emotional and behavioral problems in medicine are those arising from chronic dependency. As a basis for disturbance in health, chronic dependency is often concealed and goes unrecognized unless the doctor is familiar with the usual signs and symptoms of its presence. Not infrequently the dependency behind one mental mechanism or another continues to go unrecognized until in an advanced stage when the damage to the personality is beyond repair or control. To prevent this from occurring, the physician should have a reasonably sound understanding of what comprises zones of emotional healthy and sick behavior within the realms of his practice. Chronic dependency will not continue to go unrecognized if the physician is on the alert to its presence.

In discussing chronic dependency as a cause of difficulty in adjusting to the demands of an adult life, it may be well to review briefly the earlier developmental years of the individual as they relate to this particular area. The child starts life by being totally dependent on the mother, then on the environment which is solely that of the parents. After the first year or so, the child begins to reach out into the environment that extends beyond the confines of the parents and home. During the earlier years of childhood, the three considered major needs are those of love, security, and support, all dependency in nature. The environment of the child during the first few years being largely that of the parents, naturally it is from that direction these earlier needs are fulfilled. The manner and extent to which these needs are met in infancy have far-reaching influence on the individual's dependency characteristics of adult years.

Every child's long awaited ambition is to become an adult wherein he envisions independence with unlimited freedom. In the process of reaching the capacity of self-reliance for adulthood, the ego strength, sense of security, and independence are developed, but not the unlimited freedom with respect to others. In this drive for maturity, the individual must conquer the need arising from the pleasure of being babied and accept the reality demands of doing for others. The child, whose parents interfere with this developmental process to make a mature adult, regardless of how physically and intellectually strong he may be, will still desire the support which he never outgrew. These desires can rarely be gratified in adult life, as it is extremely difficult to make up later for the effects of such deprivation. What the individual had or wanted from parents as a child rarely will be forthcoming from friends and associates in later years. When the desire to be dependent and protected comes in conflict with the wish to be independent and mature in an individual whose early childhood emotional needs have not been satisfied, there arises an inner sense of weakness and inadequacy which reflects adversely on adult adjustment.

If the dependency needs are adequately met throughout infancy, as the child's personality develops he will willingly relinquish

them prior to adulthood. In that he is satisfying his dependency needs in an adult manner, he can tolerate more and more frustrations of adult competition, periods of discomfort and illness with regressing. If emancipation from the parents has been gradual, suited to the maturing capacities of the child, and in the presence of praise by the elders, he will not find it necessary to cling tenaciously to his earlier dependency needs. He will have acquired satisfying technics of his own in meeting environmental pressures. This abandonment is greatly assisted by the process normally occurring in the child-parent relationship, that of identification, wherein the child gains strength and security by establishing a dependence on one whom he considers stronger and independent. This process is a necessary adjunct to the development of security in later years.

Over and beyond dependency, there are other traits normal to childhood, those of being selfish, parsimonious, sadistic, messy and unclean, the nature of which is not readily acceptable if continued into adulthood. These traits, as is dependency, are normally relinquished or reorganized in their method of expression as ego strength, and social maturity; independence comes from the experiences in an exchange of give-and-take with associates of relatively the same age and environmental background. The over-protected and over-indulged child has not been permitted this opportunity for development.

The child who did not have his early dependency needs fulfilled, and was not permitted the experience necessary to eventually satisfy these needs, will continue to be dependent in adult life. When dependency persists, the individual is markedly handicapped in his ability to cope with the demands of an adult environment. He will reveal various forms of inadequacy for which he is readily prone to openly blame others. That individual resents anyone upon whom he must depend, and in periods of illness, with its enforced dependency on others, is likely to channel hostility in the direction of the person who is trying to help him.

There is a large number of individuals who, instead of being over-protected, have been encouraged, forced, or shamed by circumstances to be so-called independent before they were chronologically and emotionally ready. The parents, in their innocent desire for a "little man," push the child too rapidly for his early dependency needs to be sufficiently satisfied. The child then represses and over-compensates for this deprivation in an effort to gain his parent's approval, to be their "little man," and protects himself against a painful awareness of his unresolved dependency. This type person is later prone to conceal unfulfilled dependency needs behind a false front of apparent independence, but these needs will sooner or later be revealed in the presence of his immaturity.

The over-protected and over-indulged child has a sense of security in the home, but that security does not transfer to the stress of growing up and meeting the demands of life outside the home. Being unprepared to enter areas of competition and having little respect for others, he is not accepted by those whom he comes in contact. He interprets this as rejection and reacts in a hostile and aloof manner, only to make matters worse. He then views the world as generally hostile and tends to retreat to the protective confines of his home. This pattern of behavior might possibly suit the parents just fine, but does not contribute to learning technics leading to an ability to more adequately meet the outside world. In later life this individual is unable to tolerate his environmental stresses without slipping back to his earlier immature dependency state.

This particular type individual not infrequently forms the basic pattern of an alcoholic in later years. His chronic dependency needs going unfulfilled, he encounters environmental stresses that give rise to tensions for which he has a poor capacity to tolerate. He may then turn to alcohol, barbiturates, or tranquilizers in an attempt to relieve his anxiety. The factors responsible for the preferential use of alcohol will vary, but such a dependent individual is usually relatively unable to control his impulses and tends to seek immediate relief of tensions and anxiety created thereby without sufficient regard for the consequences. Alcohol is all too readily available and socially acceptable. Further, this type of dependent personality is not unlike that seen in individuals who turn to the habituate use of such drugs as narcotics, amphetamine, tranquilizers, and barbiturates.

In cases where the child's parents may

have been over-concerned in matters of health, the child soon learns that this area is a device which he can use to advantage in various unpleasant and deprived situations. In later years, such an individual, without being aware of it, is prone to exaggerate and magnify relatively minor complaints when he encounters environmental stresses. Using symptoms as an unconscious lever to gain attention, avoid discomfort, and control the situation, the individual may go to the extent of becoming incapacitated.

Many physicians steer clear of patients with emotional and personality disorders, particularly those with obvious chronic dependency traits. In treating such conditions, the physician may feel he encounters a distinct challenge to his position of authority by leaving him little in the way of a concrete and unchallenged approach, such as prescribing medicines and diets. It is possible for the physician to do his daily work with complete confidence as to a feeling of authority in the physical and organic realms, but this does not hold true for the psychologic and functional areas. He has had years of training and experience in physical medicine about which the laymen have little knowledge. That gives him a position of authority and people tend not to dispute his word. On the other hand, every individual has had his own personal experience in the area of psychologic medicine involving problems of emotion and human behavior, and each has his own criteria for evaluation and does not hesitate to express them, even though they are without scientific validity. Not desirous of having his expressed opinions questioned, the physician will frequently shy clear of broaching psychophysiologic causation of illness, and instead of openly and with confidence discussing the involved emotional factors with the patient, he may brush the situation aside with a pseudophysical approach in the form of a prescription and a reassuring word. Such temporizing leads to increasing the neurotic illness and chronic dependency on doctors. The patient then "goes the rounds" with a strong, and partly justified resentment that he has not found the real help he needs. A functional complaint of a patient may stir up a negative, resentful attitude on the part of the physician in the form of an unconscious defense mechanism. He may view such a patient as "just neurotic" and prescribes tranquilizers for an indefinite period, when all that is actually required is a healthy, friendly curiosity about the emotional reactions of the patient and a searching attitude toward his own emotional self.

The physician may find it difficult to be objective and tolerant with individuals who have problems arising from chronic dependency. The physician, being hard-working, resents the able-bodied adult who does not carry his share of adult responsibility. Should the physician reveal his irritation in such situations, the dependent patient interprets the reaction as rejection by the parent substitute. This only confirms the opinion of the patient that he is not loved but only protected against his helplessness, which in turn strengthens his tendency to remain helpless. Dependence carries with it resentment and helplessness, and consequently the patient may feel and express hostility toward those depended upon. If such hostility is in the direction of the physician, it may be misconstrued as ingratitude.

The typical chronically dependent patient may at first cling to the physician in a very flattering manner of having found someone who understands his problems and in whom he has confidence. The treatment situation goes along in what appears to be a very satisfactory manner with this initial period of patient-doctor relationship producing a mutual optimism with the patient unconsciously developing the feeling that at last he has found someone who will take complete control of him in the fulfillment of his immature needs. Sooner or later, the patient begins to realize that as an adult no one will furnish the all-inclusive maternal care which was forthcoming in infancy. He then starts doubting the permanence of this new relationship and, in a child-like manner, begins to test the parent substitute. When this testing goes beyond the ability of the physician to fulfill the immature demands, the patient, feeling rejected, will act hostilely and possibly break off the so-called treatment relationship. If the physician, however, foresees what is taking place, controls his irritation and continues to treat the patient in a kindly, impersonal, but sympathetic manner, he may help the patient to grow maturely and succumb less to his chronic dependency needs.

Many physicians are untouched by the strong emotionally charged feelings around them. It is necessary for them to realize, however, the difference between when they have incurred justifiable resentment and when troubled feelings are being worked out in their direction in the form of transference. In working through emotional problems with patients, a certain amount of therapeutic heat may have to be engendered before results are obtained.

If by chance the physician is over-sympathetic toward the patient and tries to supply the deprived dependency needs of earlier years, he will soon realize this is impossible and that he is in a hopeless situation. No one can compensate to an adult for deprivation of infancy needs by an over-sympathetic, or any other, attitude. The physician should attempt to have the patient become aware of his dependency needs, and try to resolve the guilt which is associated with them. The physician helps the patient most by not getting too close to him, or being over-permissive. As far as possible the physician should maintain an impersonal, attentive, understanding, and firm attitude, dealing only with the mature side of the dependent patient. In emotional disorders the treatment of dependency should be carried out in such a manner that the patient continues to recognize and accept his dependency as his own burden, and that the doctor is giving temporary help to him for such parts of his troubles that he cannot manage for the time being.

It is but a small part of the problem to say that a chronically dependent patient comes to the physician for relief of tension, restlessness, or hostility. Somewhere within the mental structure of this type of patient there exist mental conflicts causing the emotional state which in turn is bringing about varying degrees of difficulty in forming and maintaining an adult environmental adjustment. These individuals are continually seeking to escape reality in that they feel unable to measure up to its demands. Indeed, depriving the patients of their dependency needs without treating the basic condition would not constitute a solution to their problems, for these needs would, in time, be transferred to some other form of emotional illness, starting them on their useless and needless rounds of physicians.

Problems of Epidemiologic Surveillance in a Program of Vaccination with Live Attenuated Polio Virus*

G. M. ERICKSON, M.D., A. W. MENZIN, M.D., L. B. CLAYTON, M.D., and M. EUGENE FLIPSE, M.D., *Miami, Fla.*, and A. V. HARDY, M.D., *Jacksonville, Fla.*

The authors outline a program for the immunization of the population of a metropolitan area with live attenuated polio vaccine.

Introduction

THE DADE COUNTY COMMUNITY POLIO PROGRAM was undertaken by joint sponsorship of the University of Miami, Dade County Medical Society, and the Dade County Health Department. It was set up to begin on Feb. 15, 1960, and to terminate on April 30, approximately 12 weeks later.

Within the boundaries of Dade County there are 27 urban municipalities, some suburban areas and a comparatively small rural population.

Geographically, the peninsula of Florida is an emerged part of the continental shelf. For the most part the land is above sea level, but there are many low swampy sections in this terrain.

Dade County is located in the Southeastern part of the peninsula and is bounded on the East and South by the Atlantic Ocean. It is a subtropical area, at about the same latitude as Canton, China. It is 300 miles south of Cairo, Egypt, and over 400 miles south of San Diego, California.

In most areas within Dade County the socioeconomic level is above average. At present time, the population enumeration is approximately 920,000. The trend of population growth is sharply upward. It is continuing to expand 7% annually.

The people of Dade County place a high value on good health practices. The quality of medical care facilities in the area is very good. Serious enteric diseases are relatively uncommon. In recent years only two to five cases of typhoid or paratyphoid fever would represent the annual incidence. The neonatal death rate for the year 1959 was 22.

It was the intent of the planners of the Dade County Community Polio Program to immunize every resident in the area less than 40 years of age. The total number in this age group was estimated at about 540,000.

Methods

It was decided from the outset that this would not be a controlled study and no placebo group was to be used. All feasible ancillary studies of a scientific nature were given a great deal of consideration. Those that could be done within the limits of available funds and personnel were then designed to become part of the program.

In Dade County paralytic poliomyelitis is an endemic disease. Its incidence varies greatly from year to year. The attack rate per hundred thousand in 1954 was 18. In the low incidence year of 1957 the attack rate was 0.75.

Mortality due to this disease is seldom high.

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†From the Dade County Department of Public Health, the Section of Preventive Medicine and Public Health, University of Miami School of Medicine, and the Dade County Medical Association, Miami, Fla., and the Florida State Board of Health, Jacksonville, Fla.

The Dade County Community Polio Program, 1960—supported in part by a grant from Lederle Laboratories, a Division of American Cyanamid Company.

Of 108 cases in 1954 there were 8 deaths. Of the 6 cases in 1957 there was only 1 death.

The seasonal pattern is unpredictable. However, in most years, the peak is reached in August or September and the low incidence months are January, February and March.

Approximately 13% of the Dade County population is nonwhite. Until 1958 and 1959 there were few cases of paralytic poliomyelitis in the nonwhite population. In both these years, however, there has been an entry of paralytic disease in nonwhite children less than 5 years of age.

The immunologic status of this community was considered very good since sustained effort had obtained wide acceptance of Salk Vaccine. Epidemiologic evidence had indicated that paralytic disease was increasing its attack rates in those vaccinated in 1959. It was disturbing to find that 14 cases of paralytic disease had occurred in those who had received 3 or more doses of vaccine. Of these 14 cases, 2 died.

Since the evidence at hand was insufficient to provide denominators that could be used for the immunized and nonimmunized groups, attack rates could not be established with acceptable accuracy.

To learn with greater precision the immune history of the population a prevaccination program was designed to obtain needed information. A modified quota sampling technic was to be used for about 1,500 households representative of high, middle and low socioeconomic groups.

The method was by interview and serologic samples. All blood specimens drawn were processed by centrifugal extraction after clotting. The resulting serum was then stored at freezing temperature until a matching sample could be drawn from the same donor after the conclusion of the vaccine program. The material collected would then be tested as paired sera.

It was appreciated that only a change in an individual donor's immune status could be reported when it occurred. No interpretation could be given to these conversions since it could not be determined whether or not immunity noted was produced by natural infection by a wild virus or secondary infection by an attenuated one.

Some judgment could be made about natural infection as reflected by the serologic survey if those who did not participate in any Salk immunization were considered as a separate group. Any immunity demonstrated would be that which had been naturally acquired.

The interview data was considered of great epidemiologic value since it reflected the immunologic history of a carefully designed sample population pertinent to killed virus polio vaccine as well as other artificial immunizations.

Without a control group other ways of obtaining contrast with the Dade County population were looked for. The most obvious comparisons were the incidence of paralytic polio in other populous areas in the State of Florida as well as data from Southeastern states and the United States as a whole.

The secondary alternative for contrast appeared to be one in time. By setting a sharp cut-off date for the termination of this program, an observer could obtain a "during" and "after" impression. After 30 days elapsed it was felt that cases that would be termed "Associated Disease in Vaccinees" would be eliminated. This would simplify surveillance to the extent that it would remove this type of case from the background.

The sharp cut-off date would also serve to give a "during" and "after" scrutiny to the aseptic meningitis syndrome. Data being collected will indicate the correlation, if any, between feeding vaccine and the incidence of this illness.

In general, surveillance during an immunization program with live polio virus would differ from usual surveillance in its degree of intensity. Minor reactions would be accepted and recorded for adequate follow-up. Everyone understood that practicing physicians in all types of medical care needed sensitizing that would render them very aware of the implication of any disease that involved the central nervous system.

To accomplish this, letters were circulated to all physicians indicating the reporting protocol. Announcements were made at Medical Society Meetings to give further emphasis to this need. Special letters were sent to pathologists. Another special letter was sent to the Medical Examiner.

A decision was made to redouble investigations at the two isolation wards in the community without attempting to include additional hospitals for epidemiologic rounds.

This greater degree of watchfulness also extended to the collection of laboratory specimens. Samples that were previously not included were now sought, and some specimens that were gathered only once now became collected serially. Besides differing in degree from former surveillance, there were significant departures in this program than those posed by a killed virus program.

When live virus vaccine is used its communicable nature is recognized and accepted. In a program employing killed virus vaccine there is no acceptable or anticipated level of spread. Any infective transference would be accidental and an occasion of unpleasant surprise.

Another item of interest is the means of immunization. The provocative factor of needle injection, hypothetical as it may be, is not a consideration when vaccine is fed orally.

In evaluating any program numbers become exceedingly important. Consistent with expectations, it could be anticipated that participants in an oral vaccine program would be far more numerous than those who would be immunized by the parenteral route.

The epidemiologic implication is that even if vaccine antigenicity in an oral program were not as great as that of a parenterally administered product the greater over-all acceptance would more than negate an antigenic disadvantage. When the idea of imparting herd immunity by gut replication of virus is also weighed, the advantages of an oral program give great immunologic promise.

During this live virus polio immunization program all of the vaccine supply passed through one channel. When killed virus had been used as an immunizing agent there were many sources of supply. In compiling data, this distribution by a single channel gives a self-apparent advantage.

At the onset of this program the question of safety of the vaccine was not considered to be in doubt. Despite this assurance, that had been substantiated by prior trials, surveillance was slanted to detect any evidence that would indicate the presence of a disease causing agent.

In particular, patterns were looked for. Would there be secondary attack rates? Would there be an increased incidence of less se ious disease in vaccines, such as the aseptic meningitis syndrome? Would there be a large number of untoward minor reactions associated with vaccine ingestion?

Effectiveness of the vaccine used in the Dade County Program was a most important consideration. To be sure of the product's potency, samples of the vaccine were drawn for laboratory testing, both pre- and after feeding.

Acceptable proof of effectiveness can be established by observing attack rates over a long period of time in those vaccinated. Serologic evidence will furnish a more immediate answer in terms of conversion as determined by pre- and after feeding blood sampling.

No attempt is being made to measure interference by other enteroviruses in this program. Since the product used is a trivalent vaccine it is most unlikely that interference by wild polio virus could be detected. This possibility seems even more remote when the unreliability of markers in current use is considered.

Despite a lack of trust in marker identification, all isolations from any cases of paralytic disease will be subjected to marker study.

There is no provision for explaining vaccination failures in the scope of this study, but all cases that may contract paralytic disease 30 days or more after vaccination will be so classified and reported.

The concept of a program of this kind extends beyond questions of safety and effectiveness of vaccine to the person vaccinated. In terms of surveillance this means that each household contact of an index case, whether severe or mild, must be surveyed. The next step is that of applying an appropriate degree of surveillance whenever illness is discovered in a household.

Another critical measure would be to estimate the incidence of illness against days of exposure of associated unvaccinated persons in the community. There are some inherent difficulties in attempting to do this. The first objection is that during a vaccination program the areas of spread represent a mosaic pattern rather than a homogeneous background.

The second objection is that the force of exposure is applied in different degrees to different areas of the community. If needed, a retrospective study can be designed to give a precise measure of illness in those not vaccinated who remained as household contacts of vaccinated persons. All who were vaccinated within a household could be sorted and tabulated. (Data on IBM cards.)

Many school age children were to be fed vaccine in schools, ahead of the scheduled feeding of their preschool siblings. The unvaccinated siblings of preschool age who remained exposed to vaccine spread number more than 15,000.

From the data that can be made available a reasonably critical measure of any illness associated with possible vaccine spread could be deduced. The group of preschool children is a susceptible one, and it would be difficult to maintain that household exposure would not be more intense than over-all community exposure.

It was well understood by this program's sponsors that attenuated polio virus was likely to circulate in this community. Budget limitation curtailed any large scale effort to measure this spread.

A study of sewage sample was designed to give some impression of virus circulation. Seventeen sampling points were selected where the effluent was from residential areas of a stable population. Points that might contain industrial waste or discharge from commercial laundries were avoided.

The collected sewage samples are now being stored in a deep freeze. When funds become available some quantitative data may become available that would perhaps correlate virus shedding with vaccine feeding and detect the circulation of other enteroviruses in the community. If new markers are discovered perhaps circulating attenuated virus and wild virus can be distinguished in these samples.

At the onset of this program, a decision was made to eliminate such disease classifications as "nonparalytic polio" and "abortive poliomyelitis." In classifying paralytic poliomyelitis the categories of bulbar, spinal, and bulbospinal have been retained. Each classification is further designated as being "with residual" or "without residual."

The definition of aseptic menigitis in the Dade County Program Protocol is: "A disease affecting the meninges and producing symptoms referable to the Central Nervous System, without bacteria in the spinal fluid, where not less than 20 white blood cells are counted in a spinal fluid examination."

Cases of aseptic meningitis are then classified as associated with whatever agent is found or if none is found as "Aseptic meningitis syndrome—no agent isolated or identified."

Whenever possible, repeated fecal specimens or rectal swabs are obtained in any case showing involvement of the central nervous system. Throat washings are also obtained whenever feasible.

Blood specimens are drawn during the acute and convalescent phase of the patient's illness. When a lumbar puncture is done, some of the material is reserved for an attempt at virus isolation.

Even though no other illness, except that of the index case, is reported within a household, stool specimens from all household contacts are being collected and held in frozen storage in the event that they may be contributory in a baffling case. Laboratory work is being done by more than one laboratory on the same specimens in an attempt to validate findings.

Blood samples have been drawn both before and after vaccination at a three week interval to minimize the likelihood of a rise in titer induced by natural infection.

Clinical evaluations of all cases occurring in Dade County are being made by qualified physicians. Each hospital has established consultant panels of unquestioned reputation and ability. Provision has also been made to furnish clinical consultation for patients who would be subjects of surveillance, even when they are not hospitalized.

To accomplish very detailed surveillance during this immunization program, forms were designed for three levels of surveillance:

The first one deals with minor complaints, usually made by telephone. The complaint may be made spontaneously by a person who has taken vaccine, or it may arise in a physician's office. This form is designed so identifying data can be recorded by a clerk and follow-up information solicited by a physician.

The second and third level of surveillance

is recorded on an identical form. It is termed second level surveillance if it is done by a public health nurse. When done by a physician it becomes third level surveillance.

The point of departure selected depended on whether or not the patient was subjected to a lumbar puncture. Prevailing thought was that any patient who underwent lumbar puncture required this procedure in the judgment of his attending physician. It was further considered that this reflected clinical evaluation of a rather serious type illness—therefore, one subject to comprehensive surveillance.

The appropriate forms appear in the appendix of this manuscript. Any questions about their composition will be answered at the conclusion of this paper.

A practical observation is that when epidemiologic surveillance is intensified more personnel are needed. Our program is currently being conducted by two physicians and a full-time public health nurse. Two additional clerks were also needed.

Early problems in the conduct of the surveillance phase of the program became apparent only with experience. The greatest single difficulty was the collection of specimens. Although this seems like a routine procedure, especially with hospitalized patients, this was far from the actual situation.

Specimens were discarded because there was no handy place to store them. This was corrected in one hospital ward when the program sponsors purchased a deep freeze for this specific purpose and placed it in that hospital ward. Usual labels were of little value. Specimens continued to be misdirected until specific labels were designed for this program. The more places or collecting points we had to deal with, the more loss of specimens we encountered. This difficulty was solved by employing a competent person whose major duty was the surveillance of specimen collection.

In closing, three studies that parallel our surveillance efforts should be noted. An enterovirus study is being conducted by the Department of Pediatrics, University of Miami and the Communicable Disease Center. Its purpose is to attempt to learn of some of the enteroviruses circulating in the community. Rectal swabs are being taken from well children less than 5 years of age and a sub-sample of these are furnishing blood for serologic examination.

The Chief of the Infectious Disease Section, Department of Medicine, Jackson Memorial Hospital, is currently studying Arbor Viruses in this area. Specimens from surveillance subjects within the polio immunization program are being included in this laboratory surveillance work.

The last but very important study under way concerns the sociologic implications of the Dade County Community Polio Program. It is evaluating matters such as acceptance, motivation, and related behavior patterns. Much information of value in planning future health programs should evolve from this study.

Preliminary Results

Since the compilation of this paper data has become available that will be of great interest to all who are concerned with planning future immunization projects.

As an over-simplification of the Dade County Polio Project it could be stated that this undertaking was begun in a population that demonstrated serologic immunity (acquired by natural infection) at a level of 80 per cent. Salk immunizations over a 5 year period had added another 10 per cent. The intensive use of oral vaccine added only 6.5% to this cumulative 90% by way of serologic evidence of immunity.

Of course this does not take into account the tissue immunity that may have been superimposed by replication via the gut, nor do such crude statistics pinpoint the areas of great susceptibility that exist within the population.

This material is now known as it applied to our study, and it can be postulated that in various stratifications by age group and other identifications that a certain number of immunizing doses will be required to close one immunologic gap. It goes without saying that the rewards will be great where numerous immunologic gaps exist—as in the very young. In other segments of the population the returns would be so limited that immunization would be impractical.

This type of information is intriguing to those concerned with program planning and we can refer you at this time to two comprehensive papers that deal at length with these

TABLE 1

TYPE II POLIOVIRUS NEUTRALIZING ANTIBODIES RESULTING FROM NATURAL INFECTION DADE COUNTY 1959 and 1960

Age Group in Years	*1950**		*1960*	
	Ratio	*%*	*Ratio*	*%*
0-4	5/21	24	3/10	30
5-9	9/18	50	17/24	71
10-14	17/24	71	12/14	86
15-39	90/113	80	61/71	86
40+	40/49	82	200/220	91

*Adapted from Paul, et al., Am. J. Hyg. 56:232-251, 1952.

aspects of the Dade County Polio Project. Both are being presented at the current meeting of APHA in San Francisco, one by Eugene M. Flipse, Professor of Medicine, University of Miami, and the other by Warren R. Hoffert, Director of the Miami Regional Laboratory, Florida State Board of Health.

In Dade County we have experienced great difficulty in getting blood specimens in the O-1 age group which would be the one most likely to yield the most triple negative titers. For this reason we call your attention to this lack of information and point out that data based on serological evidence has as its youngest group that from age 1 to 4 years.

Table 1 is presented to show that neutralization tests done by the pH method in 1960 in Miami correlate well with a survey done by Paul, et al., in 1950. Here the results shown are for the unimmunized and represent only serological evidence of natural infection with Type II polio virus. The 0-4 age group is shown in this table to conform to Paul's data.

TABLE 2

ANTIBODY STATUS BY AGE GROUP AMONG A RANDOMLY DRAWN SAMPLE OF THE POPULATION—DADE COUNTY, FLORIDA, 1960

Age Groups		*1-4*	*5-9*	*10-14*	*15-24*	*25-39*
Per cent in each age group with	No gaps	49	77	88	86	84
	One gap	24	15	10	7	11
	Two gaps	17	8	2	6	5
	Three gaps	10	.8	.5	.9	2

By age groups antibody status can be shown in the quota sample as shown in table 2.

It is apparent that the lowest age group presents 88 gaps in 102 persons. Here it would be possible theoretically for 1.15 doses to fill one immunologic gap. In the 25 to 39 group, however, it would require almost five doses to fill one immunologic gap.

In addition to more detailed serologic presentations, the papers to which we have previously referred will contain much data on Salk vaccine use in the Dade County population as well as a report on some findings gathered from a Social Science Study of this project. They will shed much light on questions that constantly present themselves to those responsible for giving form and direction to public health programs.

Summary

Some thoughts about problems of surveillance pertinent to the Dade County Community Polio Program are presented to show how some of these measures differ in intensity from usual surveillance, how they differ from programs that have used killed virus vaccine and some special problems that they pose by their communicable nature.

In addition reference is made to some data that has become available through serologic surveillance to this date. A few ideas are put forth on how surveillance data can be useful for those concerned in planning programs that entail similar problems. Reference is made to two comprehensive papers that will give detailed reports on serologic results, Salk vaccination history of this population, and some findings of a Social Science Study on this project.

Acknowledgment: Grateful acknowledgment is made to: W. R. Hoffert, M. M. Sigel, N. J. Schneider, T. E. Cato, F. J. Evans, A. L. Johnson, and J. O. Bond.

Otitis Media with Effusion in Children*

GUERDAN HARDY, M.D., *St. Louis, Mo.*

One using antibiotics in the treatment of otitis media, especially, as well as for other upper respiratory infections in children, should use careful follow-up to be assured there is no remaining effusion in the middle ear.

OTITIS MEDIA with effusion has been noted more frequently in recent years and the increased number of cases is the result of several factors. A casual survey of otologic literature offers evidence that there is a greater awareness of this condition on the part of physicians.

The hearing tests made in schools have uncovered many instances of earlier deafness and parents have been informed of hearing loss in their children. Television has done its share by providing a crude hearing test in the home. Many parents have stated they suspected a loss in hearing because the television was operated at full volume constantly.

The practically unrestricted use of antibiotics, often prescribed without seeing the child with otalgia, has been a contributing factor. Formerly, otitis media usually ended either with spontaneous rupture or with incision of the eardrum and drainage of the middle ear. At the present time, incomplete resolution may be the result of too much reliance on antibiotics and a lack of surgical drainage.[1] Inadequate antibiotic therapy does not have the desired bacteriocidal effect and has often resulted in attenuation of the bacteria. Surgical drainage of the middle ear by myringotomy has not been utilized often enough and, as a result, secretion has remained in the tympanum indefinitely.

New types of avirulent infections, and virus infections, have also been considered responsible for more cases.[2,3] Constantly recurring ear infections, with or without hearing impairment, have brought many to the offices of the otologist. If there is involvement of both ears, loss of hearing is more noticeable and medical advice is sought sooner. Many times unilateral otitis media has been discovered on a routine examination when ear trouble was not the primary complaint.

Etiology

It is believed that anything interfering with the normal physiologic state of the eustachian tube, or any obstruction to it, may produce middle ear effusion.[4,5] Hoople[6] has stated that any condition which can induce swelling and closure of the eustachian tube may be an etiologic factor and, in addition to lymphoid tissue, he mentioned endocrine disorders, cardiac insufficiency, and disorders of the autonomic nervous system.

Perlman[7] has found no parallel between the amount of adenoid tissue and the presence of effusion. Davison[8] has directed attention to lymphoid hyperplasia arising from conditions other than infection, and referred to such factors as low gamma globulin level, allergy, hypothyroidism, and obesity.

Allergic conditions have been considered as causes of otitis media with effusion.[9,10] Occasionally there may be a history of hay fever, hives, asthma, or sneezing spells, but more often there is nothing in either the history or the physical examination to make one suspicious of an allergic diathesis. The concensus of opinion among otologists seems to be that while allergic conditions may produce an otitis media with effusion, allergy *per se* is not an important etiologic factor.[11]

The combination of lymphoid tissue and infection in the nasopharynx has received most of the blame and attention from otologists.[5,11] Still, we find otitis media with effusion occuring in children who have had an adequate adenoidectomy and no obvious evidence of infection. Perlman[7] examined serial sections made through eustachian tubes and demonstrated

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subepithelial tissue distal to the pharyngeal end of the auditory tube and also lymphoid tissue extending over the torus. This suggested that distribution of the lymphoid tissue in and about the nasopharynx may be as important as the quantity of lymphoid tissue there.

Diagnosis

The diagnosis of otitis media with effusion can be more difficult in a child than in an adult because children seldom complain of ear sensations, with the exception of pain, and often an adequate history cannot be obtained. Only occasionally will a youngster state that his ear feels blocked or describe changes in his hearing. At times a child, with his limited vocabulary, will use the term "pain" when he is trying to describe pressure or fullness in the ear.

In the very young, hearing tests made in the office are usually inaccurate and inconclusive. In children 6 years of age or older, tests can be made with a degree of accuracy, and the hearing may be found to decrease 10 to 30 decibels or more.[12] This decrease in hearing acuity may be present in all or only in certain frequencies.[13,14] Several authors have reported that the loss of hearing occurs primarily in the higher frequency range. Others have stated that the audiogram is not a reliable guide to the diagnosis and have claimed that occasionally the examiner is led astray because the audiometer tests indicate a perceptive deafness.[5,15] I believe the reverse is true also, and that it is most important to carefully evaluate the results of tests in order not to overlook a perceptive deafness. In most instances of otitis media, carefully performed supplementary tests with tuning forks will reveal a negative Rinne and indicate a conductive deafness.

It is well known that a small amount of air can enter the middle ear by way of the eustachian tube and a temporary improvement in hearing will occur. As a result, it is possible for a child with chronic effusion in the middle ear to have nearly normal hearing at the time he is tested. However, he still has a condition which can lead to permanent impairment of hearing. I have examined children in whom the eardrums were thickened, dull, and practically immobile, and yet the hearing was as normal as one could determine in a 5 or 6 year old. However, these are exceptions to the rule.

The tympanic membrane may vary greatly in appearance. It has been described as flat, as retracted, and as slightly bulging. The color varies in descriptions from a pinkish hue to a deep blue or purple. Goodhill[15] pointed out that the diagnosis was not easy because the tympanic membrane "may appear deceptively normal." Bateman[16] described the eardrum as being normal in color but that it appeared as if it were poorly illuminated. Tremble[3] has reported that the character of the effusion, and the length of time it is in the middle ear, can alter the appearance of the eardrum. I think that this is generally true.

In serous otitis media the eardrum is likely to be somewhat retracted, pink or amber in color, and occasionally a fluid level is seen. However, when thick mucus is present in the middle ear, the tympanic membrane is more likely to be dull, thickened, and full, and usually no fluid level can be seen. It is frequently difficult to make a positive diagnosis on the appearance of the eardrum alone; therefore, other diagnostic procedures are necessary.

An examination with the electric otoscope, and with the pneumatic otoscope, before and after introducing air into the middle ear, should be routine diagnostic steps. However, the introduction of air by catheterization is not recommended for children.[1] The procedure is somewhat unpleasant, it is apt to be resisted and, once performed, future examinations are likely to be more difficult for the physician. A more agreeable and much less traumatizing method of introducing air is the continuous pressure method described by Ogden.[17] Even this procedure will be resisted by some.

One of the best aids in making a diagnosis is the study of the movement of the eardrum with the pneumatic otoscope.[1] I rely more on careful observation of the mobility of the eardrum, and on changes in the appearance of it with alterations in positive and negative pressure, than on any other single test. This examination is painless and atraumatic and can be used on children of all ages.

Needle puncture of the eardrum and aspiration of the middle ear contents, as an office procedure, should be reserved for adults. If entrance to the middle ear of a child is required, either diagnostically or therapeutically, it should be done under a general anesthetic,[1] and a myringotomy is much to be preferred

to a puncture. The incision should be made large enough to allow the insertion of a small suction tube. If the secretion is viscid, a second incision is sometimes helpful in removing it.

Preoperatively, I know of no way to determine with absolute certainty what the middle ear contains. If one sees fluid moving with a change in position of the head, or notes bubbles after inflation, there is no doubt of effusion. But behind a dull, or thickened, or opaque, or immobile eardrum there may be anything—or nothing.

Treatment

Senturia and his co-workers,[4,11] with laboratory aids, have differentiated four types of effusion and have suggested treatment for each type. Aside from the acute inflammatory diseases with mucopus in the tympanic cavity, I can differentiate, by clinical examination, only two types of otitis media with effusion in children. The first type is the serous otitis media, with a thin watery transudate partially or completely filling the middle ear. This type is encountered less frequently in children than in adults. It is noted occasionally as a complication after an adenoidectomy and under such circumstances it almost always clears spontaneously. It is likely to occur after an acute respiratory infection and usually responds to conservative treatment to the nose and sinuses, and to the administration of topical and systemic vasoconstrictors. It may also clear after a few inflations, using continuous pressure politzerization.[17] In children, inflation with a catheter is not recommended for reasons previously given.

The second type is the exudative or mucous otitis media, also referred to as "glue ear." This type, in my experience, occurs more often in children than in adults. Most authorities consider it to be the result of repeated inflammations in the middle ear, usually associated with tubal obstruction from lymphoid hyperplasia.[4,11] The mucus or glue ear will often persist in spite of all conservative therapeutic measures and removal of the mucus from the tympanum almost always requires a myringotomy and suction.

The treatment then should vary somewhat depending on the contents of the middle ear. It is axiomatic that any basic etiologic factor must be corrected. If an allergy is thought to be the exciting factor, proper steps should be taken to control or eliminate it. However, if the allergic condition is not controlled and fluid remains in the middle ear, one should proceed with surgical treatment. Any lymphoid tissue in the nasopharynx should be removed as cleanly as possible and necessary measures taken to clear infection from the paranasal sinuses. Whether surgical removal of lymphoid tissue is followed by roentgen or radium therapy to the nasopharynx depends on personal experience and convictions.

At the present time, the procedures I have adopted in handling persistent otitis media with secretion is somewhat as follows: Any necessary surgical treatment of the nasopharynx and sinuses is completed. This may include removal of lymphoid tissue, puncture and lavage of the maxillary sinuses, and antrotomy if necessary. A myringotomy is performed and the fluid is removed by suction. As a rule no polyethylene tube is inserted into the middle ear unless I am dealing with a recurrence of effusion. However, if thick ropey secretion is encountered, suction is used to clear the middle ear as thoroughly as possible, and then a polyethylene tube is inserted and left in place for about 4 weeks.

Antibiotics are not administered unless purulent secretion is encountered at the time of operation or unless suppuration develops subsequently.

Whenever there is a recurrence of effusion, attempts are always made to obtain improvement by conservative measures and these are often successful. If the condition persists, however, and myringotomy is again necessary, then it has been my routine to insert an indwelling polyethylene tube and to leave it in place for about a month. In the instances where the nasopharynx appears to be clean, I insert my forefinger into the postnasal area and break any adhesions that may be present between the torus and the wall of the nasopharynx.

It has been my observation that a tapered polyethylene tube is almost always extruded in about 3 to 4 weeks. This extrusion can be delayed by using a specially prepared tube. If one end of a piece of polyethylene tubing is placed momentarily in a flame, a rolled edge is formed. The final shape of the tube is not unlike that of a retention catheter. When the rolled end is placed into the middle ear, the tube will remain in place almost indefinitely. There is one disadvantage, however; removal

of the tube is likely to be momentarily painful to the child.

Clinical Survey

A survey was made of 100 consecutive children with otitis media with effusion. The ages ranged from 9 months to 11 years; there were 45 girls and 55 boys. The predominating symptoms were deafness with head-colds, repeated attacks of earache, and persistent impairment of hearing.

A history of asthma was obtained in 5 instances. A history of drug or food allergy, eczema, sneezing attacks, or hives was obtained from the parents of 10, but there was clinical evidence of nasal allergy in only 2 of these children.

At the time of operation, mucus was removed from one or both ears 71 times, while thinner fluid was noted in one or both ears 33 times. Sometimes fluid was found in one ear and thick mucus in the other. In 4 instances no fluid or mucus was found in the middle ear although the eardrum had an abnormal appearance.

A tonsillectomy, adenoidectomy and myringotomy was performed on 54 and an adenoidectomy and myringotomy on thirty-five. In addition, maxillary puncture or antrotomy was done 6 times. Myringotomy alone or combined with antrum puncture was performed on 10 children and tonsillectomy plus myringotomy on two. Most of the children had multiple procedures, so the operations total more than 100.

A polyethylene tube was inserted into one or both ears of 36 children and it was noted that this procedure has been done with greater frequency in recent months. One reason for the more frequent use of the polyethylene tube has been its routine use whenever there was a recurrence of fluid. Furthermore, experience has shown that patients with a "glue ear" seemed to resolve sooner and had fewer recurrences if an indwelling catheter was used initially.

Conclusion

Otitis media with effusion should not be considered a benign and innocuous condition with only temporary effects, usually clearing spontaneously, and without sequelae. Early recognition of unresolved otitis media and prompt institution of therapy are important. Although it is known that restoration of hearing to a normal or nearly normal level can follow evacuation of secretion from the middle ear, as yet it is not known how long the primary disease can remain or how long this secretion can be present before irreversible changes in the tympanum take place.[16,18,19]

Experimental work on animals[1] has indicated that viscid material in the middle ear can produce changes in air conduction and also a decrease in the threshold of bone conduction.[18] The development of microsurgery has made us more aware of pathologic changes in the middle ear, and such conditions as necrosis of the ossicles and fibrosis of the mucosa may be the sequelae of unresolved otitis media.

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Discussion (Abstract)

Dr. Ben H. Senturia, St. Louis, Mo. Dr. Guerdan Hardy has selected a very important topic for his talk and in his usual fashion has given us a very practical, clinical discussion.

I certainly agree with the statement that, for practical purposes, one is able to differentiate by clinical examination only two types of otitis media with effusions in children. But I would call your attention to the fact that there are many categories of middle ear effusions. Dr. Hardy alluded to the type which follows inadequately treated suppurative otitis media. He also mentioned the occasional occurrence of an allergic middle ear effusion, the amber-colored eardrum as-

sociated with nasopharyngeal malignancies, and the blue ear.

Dr. Hardy cautions that a complete otologic examination is necessary and that this should include otoscopic examination before, during and after continuous pressure politzerization.

Our group emphasizes the importance of aspirating the middle ear fluid into a collecting tube so adequate cytologic and bacteriologic examinations can be performed. We have described the various microscopic findings and the great importance it plays in the proper diagnosis and treatment of our patients.

Although these observations do not provide immediate information at the time of operation, the report of a seropurulent cytologic picture and a culture of, e.g., *H. influenzae*, would influence me to prescribe the proper antibiotic, if I had failed to do so immediately following operation. This added information has shortened the recovery period for many of our patients.

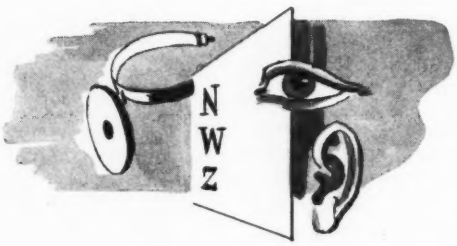
We make it a rule to perform all myringotomies on children under general anesthesia in the hospital so we may evacuate all the fluid from the middle ear whether serous or mucoid. At the same time we not only palpate the nasopharynx but also use a specially designed nasopharyngeal speculum which permits us to visualize Rosenmüller's fossae and the vault of the nasopharynx. With a small Meltzer forceps, all excessive lymphoid tissue which may obstruct the posterior nares and any infected adenoid tissue in Rosenmüller's fossae are removed.

I should like to emphasize the importance of ruling out maxillary sinus disease as a contributing factor in the development of middle ear effusions. At the time of general anesthesia, antral irrigation is performed in all patients who show an opacity of the antrum on x-ray examination.

I should like to be very positive about the role of roentgen or radium therapy for the treatment of lymphoid tissue in the nasopharynx. Although, in the past, I was a proponent of the use of the radium applicator in selected cases, I now firmly believe that radiation therapy should not be done in view of the evidence which strongly suggests a possible dangerous sequel following its use.

I feel that Dr. Hardy's suggestion that polyethylene tubes be used in all mucopurulent cases deserves careful consideration and I shall review all of our cases to determine what percentage of our mucopurulent ears failed to clear on simple aspiration.

I certainly enjoyed the privilege of discussing Dr. Hardy's paper.



The Spatial Vectorcardiogram and Ventricular Gradient in Left Bundle Branch Block with Autopsy Studies*

G. E. BURCH, M.D., and
N. DEPASQUALE, M.D.,† *New Orleans, La.*

The authors point to the difficulties in the diagnosis of cardiac lesions electrocardiographically, as myocardial infarction for example, in the presence of left bundle branch block. The spatial vectorcardiogram is of aid in this area though, as the authors indicate, the studies have been inadequate in number as well as, more importantly, in correlation with pathologic findings. They have met the latter inadequacy in this study.

THE SPATIAL VECTORCARDIOGRAM (sVCG) and ventricular gradient (G) in left bundle branch block (LBBB) have been described previously.[1-7] Yet, in each investigation the number of patients studied was relatively small and few autopsy studies were made to evaluate the complicating factors. This study was prompted by impressions formed during the past few years which indicated that in some instances lesions of the heart such as myocardial infarction might be detected electrocardiographically and vectorcardiographically in the presence of LBBB. While this investigation was in progress, Chapman and Pearce[8] reported instances in which myocardial infarction could be detected from the routine, conventionally recorded electrocardiogram when complete LBBB was also present.

This study was undertaken to investigate: (1) the spatial vectorcardiogram in 77 patients (24 autopsied) with complete LBBB; (2) the ventricular gradient in these same patients; and (3) the influence of other cardiac lesions upon the ventricular gradient and the pattern of the sVCG in left bundle branch block in order to determine whether or not these lesions can be detected in presence of the block.

Methods and Materials

Seventy-seven patients from the Veterans Administration Hospital and the Charity Hospital of New Orleans were studied. The patients varied in age from 33 to 81 years with a mean of 59 years. Twenty-six were women and 51, men; 43 were white and 34, Negro. The clinical and diagnostic data are summarized in tables 1 and 2. The electrocardiogram and spatial vectorcardiogram were recorded either at the bedside or in the Cardiovascular Research Laboratories of the Department of Medicine of the Tulane University School of Medicine. Only patients with classical electrocardiographic patterns of LBBB were included in the series. The criteria used for complete left bundle branch block were those which are generally accepted today and which were established by Wilson and associates.[9]

TABLE 1

CLASSIFICATION OF THE 77 PATIENTS WITH LBBB ACCORDING TO ETIOLOGIC DIAGNOSIS

Etiologic Diagnosis	*Number of Patients*	*Per cent*
Hypertensive cardiovascular disease	25	32.5
Arteriosclerotic heart disease	29	37.6
Hypertensive cardiovascular disease and arteriosclerotic heart disease	10	13.0
Myocarditis		
(a) Idiopathic	2	2.6
(b) Rheumatic	4	5.2
Syphilitic heart disease	3	3.9
Metastatic carcinoma to heart	2	2.6
No heart disease other than LBBB	2	2.6
Total	77	100.0

*This paper was published in *Modern Problems of Cardiology*, Academy of Medical Sciences, U.S.S.R. Institute of Therapy, Moscow, 1960.

†From the Department of Medicine, Tulane University School of Medicine, Charity Hospital of Louisiana and the Veterans Administration Hospital, New Orleans, La.

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TABLE 2

CLASSIFICATION OF THE 77 PATIENTS WITH LBBB ACCORDING TO ANATOMIC DIAGNOSIS

Anatomic Diagnosis	*Number of Patients*	*Number Autopsied*	*Per Cent of Total Patients*
Left ventricular hypertrophy	32	5	41.6
Left ventricular hypertrophy and myocardial infarction	35	15	45.4
Diffuse disease with myocarditis	6	1	7.8
Metastatic carcinoma to heart	2	2	2.6
No heart disease other than LBBB	2	1	2.6
Total	77	24	100.0

The spatial vectorcardiograms were recorded, as previously described, using the equilateral tetrahedral reference system.[10] In addition to photographic recordings of the various plane projections, wire loops of all spatial vectorcardiograms were constructed and studied. At the same time, the routine, conventionally recorded standard leads, unipolar limb leads and precordial leads $V_1 \triangleq V_6$ as well as other special leads were recorded.

The ventricular gradient of Wilson was measured for each patient as well as the direction and magnitude of the $\hat{A}_{QRS}$ and $\hat{A}_T$ and the angles between $\hat{A}_{QRS}$ and $\hat{G}$ and between $\hat{G}$ and $\hat{A}_T$. Considerable accuracy in measurement was ensured by projecting the electrocardiograms to a size four times larger than the original with an epidiascope.

The electrocardiogram, spatial vectorcardiogram, ventricular gradient, $\hat{A}_{QRS}$ and $\hat{A}_T$ were carefully correlated with clinical and autopsy data.

Results

The patients were grouped according to the cardiac lesions associated with the LBBB (Table 2). The findings are discussed according to these groups after first presenting certain fundamental characteristics of the sVCG and ventricular gradient in LBBB.

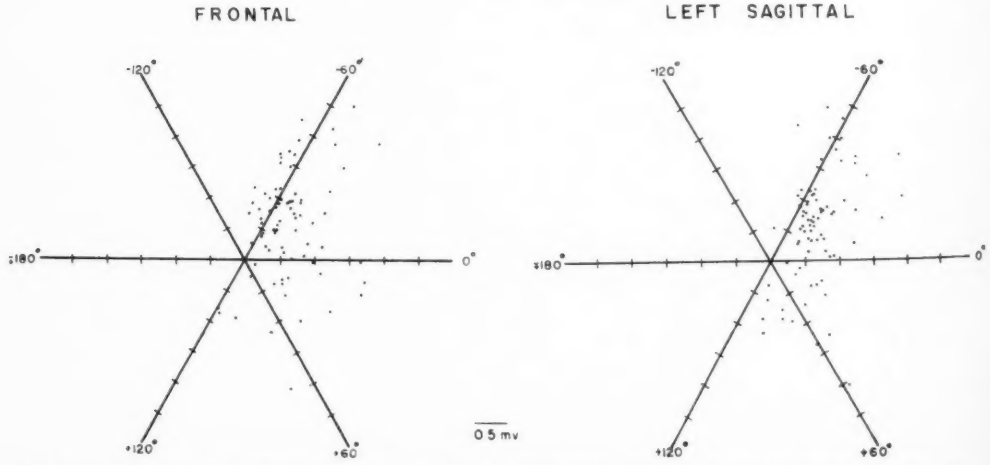
General Manifestations of Left Bundle Branch Block

The manifestations of LBBB in the sVCG and the ventricular gradient in these investigations were similar to those found in previous studies.[1-7] These are briefly discussed.

The Spatial Vectorcardiogram: With few exceptions the QRS sÊ-loop was oriented to

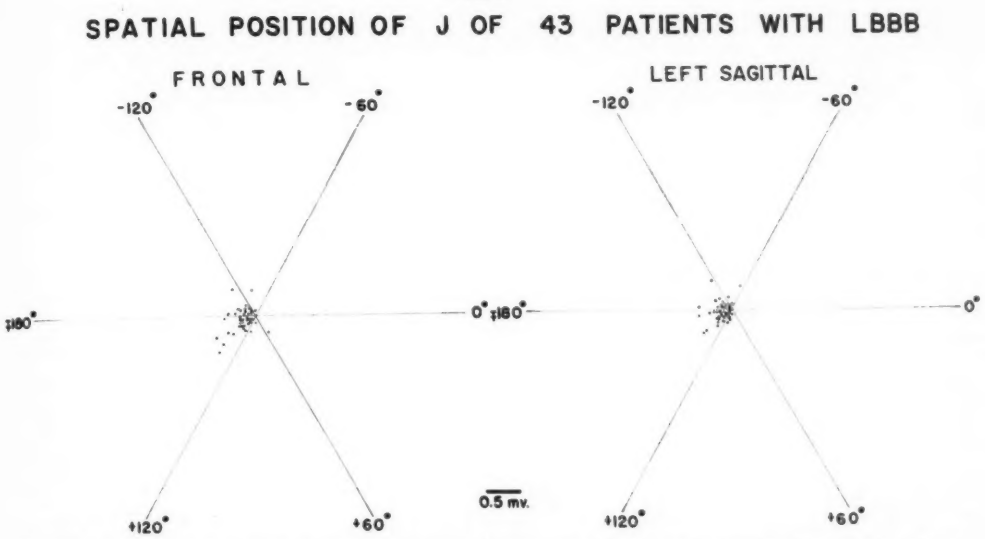
FIG. 1

MAGNITUDE AND DIRECTION OF MAXIMAL QRS VECTORS OF 77 PATIENTS WITH LBBB



The magnitude and direction of the maximal instantaneous vectors of the QRS sÊ-loops of the 77 patients with LBBB. The magnitudes of the vectors are in mv., as indicated by the scale.

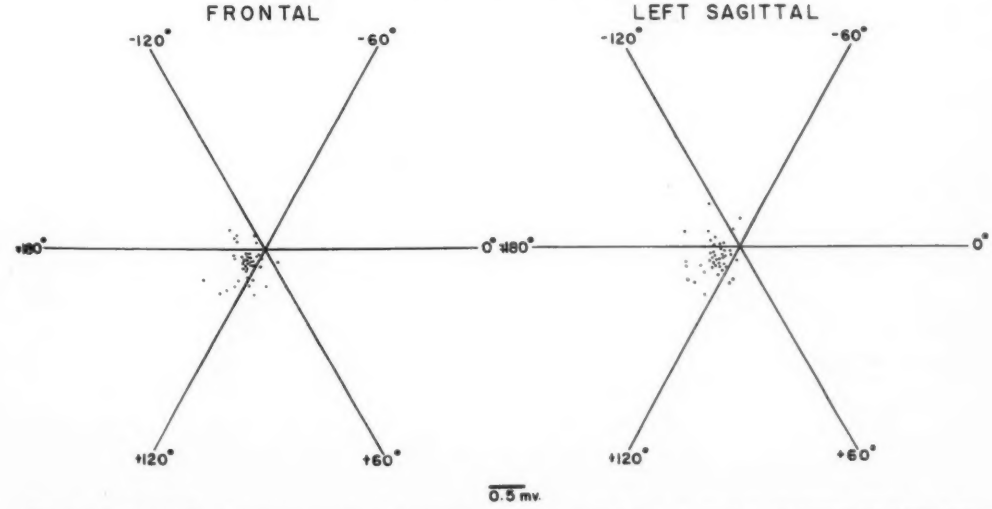
FIG. 2



The spatial position of J in 43 of the 77 patients with LBBB. The position of J could not be determined for the other patients studied.

the left, superiorly and slightly posteriorly (Fig. 1 and Table 3). Except in 2 patients it rotated slowly in a counterclockwise direction in the frontal plane projection. In most patients it was distorted but not as much as for the patients with myocardial infarction complicating the LBBB. The QRS sÊ-loop terminated at the junction, J, which was oriented to the right, inferiorly and anteriorly (Fig. 2). The T sÊ-loop was C- or horseshoe-shaped,

FIG. 3



The magnitude and direction of the maximal instantaneous vectors of the T sE-loops in 43 of the 77 patients for whom these vectors could be determined.

TABLE 3

THE MAGNITUDE AND DIRECTION OF THE MEAN MAXIMAL INSTANTANEOUS VECTORS OF THE QRS AND T sÊ-LOOPS

	Maximal Vector in Frontal Plane				*Maximal Vector in Left Sagittal Plane*			
	QRS sÊ-loop		*T sÊ-loop*		*QRS sÊ-loop*		*T sÊ-loop*	
	Direction (Degrees)	*Magnitude (mv.)*	*Direction (Degrees)*	*Magnitude (mv.)*	*Direction (Degrees)*	*Magnitude (mv.)*	*Direction (Degrees)*	*Magnitude (mv.)*
Minimal	−85	0.15	+52	0.11	−84	0.24	+107	0.14
Maximal	+120	2.94	+256*	0.90	+100	2.41	+271	0.82
Average	−24	1.08	+152	0.38	−21	1.05	+165	0.41

*For convenience when the T sÊ-loop or the $\hat{A}_T$ rotated in a clockwise direction beyond 180°, the vector was assigned a positive value in this case 256° rather than −104°.

rarely being a closed loop. It was oriented to the right, anterior and inferior to the isopotential point (Fig. 3). It resembled the T sÊ-loop previously described for left ventricular hypertrophy.[11]

Ventricular Gradient: The data obtained for $\hat{A}_{QRS}$, $\hat{A}_T$ and $\hat{G}$ are summarized by figures 4 and 5 and tables 4 and 5. The $\hat{A}_{QRS}$ was located to the left and superiorly, the mean vector being in the first sextant with a magnitude of 67 μv. s. and a direction of −17°. The $\hat{A}_T$ was located to the right and inferiorly with a mean magnitude of 44 μv. s. and a mean direction of +135°. The ventricular gradient, $\hat{G}$, was located to the left and slightly inferiorly with a mean magnitude of 39 μv. s. and a mean direction of +0.5° (Fig. 5). $\hat{G}$ in this series of patients with LBBB tended to be shorter and further to the left than the mean normal $\hat{G}$ (46.2 μv. s.[12]). The $\hat{G}$:$\hat{A}_{QRS}$ ratio for the 77 patients was less than unity (0.64). Normally, $\hat{G}$ is about twice the magnitude of the $\hat{A}_{QRS}$.[13] The angles between $\hat{A}_{QRS}$ and $\hat{G}$ were normal in 66% of the patients, whereas the angles between $\hat{G}$ and $\hat{A}_T$ were normal in only 9% of the patients (Table 5). There were considerable variations in all 3 parameters.

Comment: In general, the sVCG of the 77 patients with LBBB conformed to the characteristics described previously.[1] Differences in the sVCG were due in part to complicating myocardial lesions. These factors are discussed below. Of the complicating lesions, left ventricular hypertrophy (LVH) was most frequently encountered and was present in all of the patients who were autopsied except the 2 who had metastatic neoplastic lesions in

TABLE 4

THE MAGNITUDE AND DIRECTION OF THE MEAN $\hat{A}_{QRS}$, $\hat{A}_T$ AND $\hat{G}$ IN THE FRONTAL PLANE

	$\hat{A}_{QRS}$		$\hat{A}_T$		$\hat{G}$		
	Direction (Degrees)	*Magnitude (μv. s.)*	*Direction (Degrees)*	*Magnitude (μv. s.)*	*Direction (Degrees)*	*Magnitude (μv. s.)*	*Ratio $\hat{G}$:$\hat{A}_{QRS}$*
Minimal	−77	15	+113	5	−87	5	0.17
Maximal	+96	164	+297*	180	+120	137	1.50
Average	−17	67	+135	44	+0.5	39	0.64

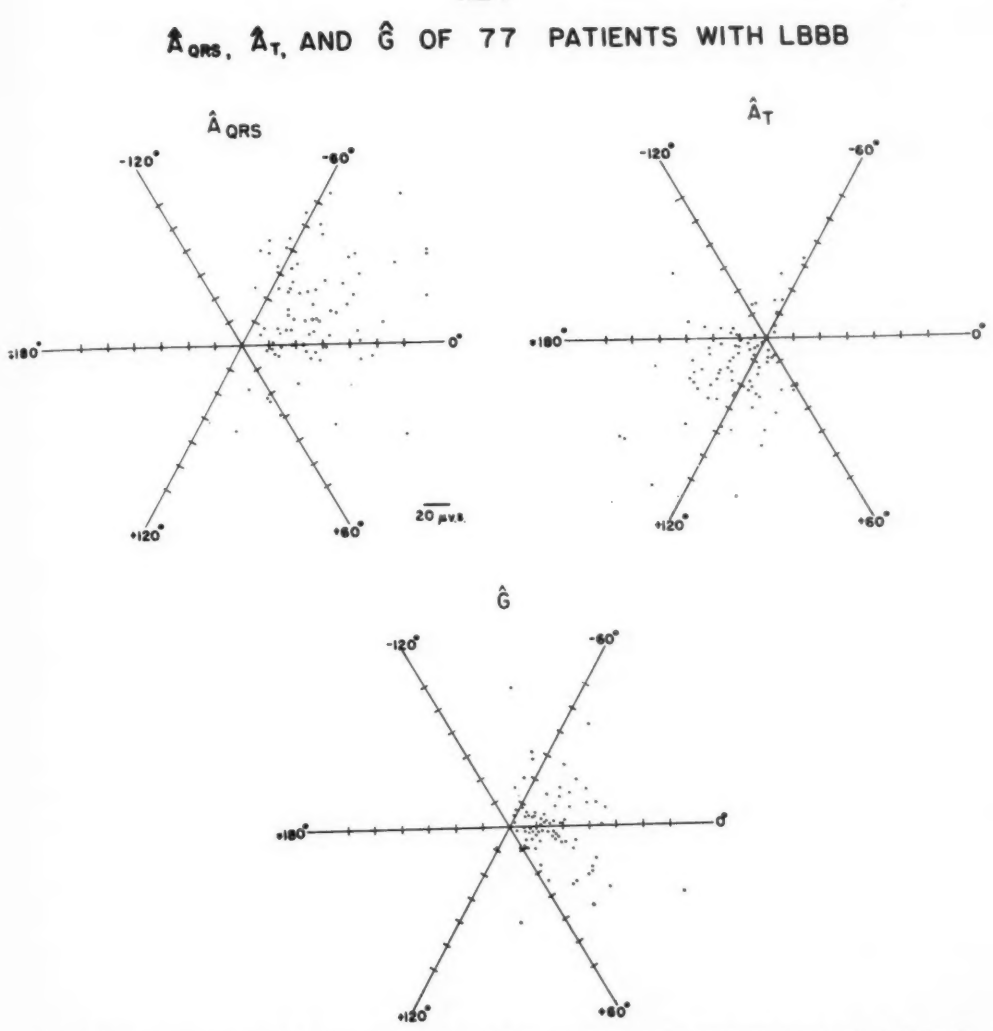
*For convenience when the T sÊ-loop or the $\hat{A}_T$ rotated in a clockwise direction beyond 180°, the vector was assigned a positive value, in this case +297° rather than −63°.

TABLE 5

DISTRIBUTION IN NUMBER OF PATIENTS ACCORDING TO THE LOCATION OF $\hat{A}_{QRS}$ AND $\hat{A}_T$ WITH RESPECT TO $\hat{G}$ AND THE MAGNITUDE OF THE ANGLES BETWEEN $\hat{A}_{QRS}$ AND $\hat{G}$ AND $\hat{G}$ AND $\hat{A}_T$

Position of $\hat{A}_{QRS}$ Relative to $\hat{G}$	*Number of Cases*	$\hat{A}_{QRS}$-$\hat{G}$			*Position of $\hat{A}_T$ Relative to $\hat{G}$*	*Number of Cases*	$\hat{G}$-$\hat{A}_T$		
		0°-35°	*36°-75°*	*>75°*			*0°-35°*	*36°-75°*	*>75°*
Right	21	16	4	1	Right	56	3	8	45
Left	56	35	16	5	Left	21	4	0	17

FIG. 4



Spot graph of the magnitude and direction of A_{QRS}, A_T and G for the frontal plane projection of each of the 77 patients with LBBB. The magnitudes of the parameters are in μv.s., as indicated by the scale.

the heart. As indicated below, it is difficult to determine the influence of LVH on the spatial orientation and configuration of the sVCG in this series of patients.

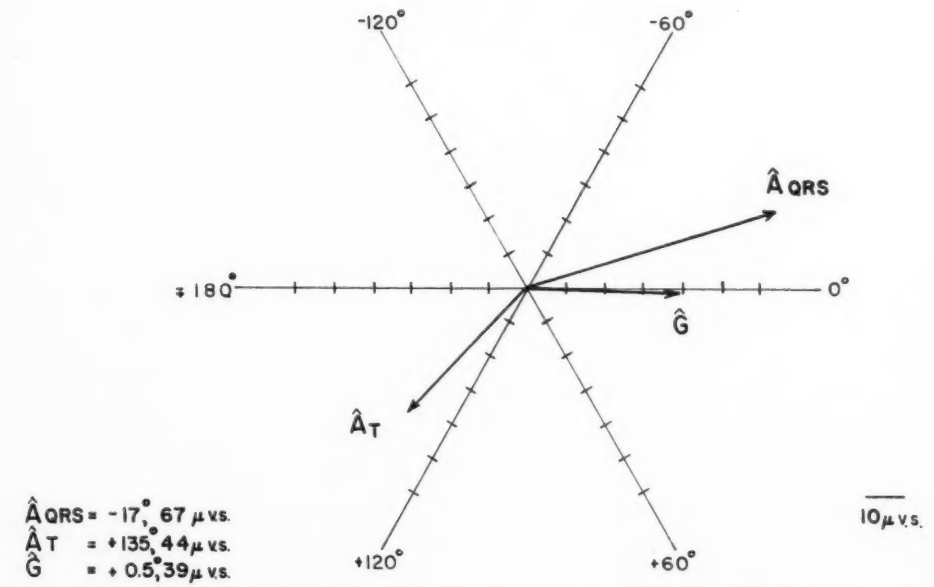
Left Bundle Branch Block and Left Ventricular Hypertrophy

Seventy-three of the 77 patients studied had large hearts with left ventricular hypertrophy. Of these patients, 32 had LVH as the principal myocardial anatomic lesion. The others had infarcts, gross scars, inflammation and other anatomic changes in addition to the left ventricular hypertrophy (Table 2).

The Spatial Vectorcardiogram: The configurations of the sVCG of the 32 patients with LVH and electrocardiographic evidence of LBBB were essentially similar to those previously described from this laboratory.[1] The QRS sÊ-loop was oriented to the left, superiorly and posteriorly, with counterclockwise rotation of the loop in the frontal plane projection (Fig. 6). The duration of the QRS

FIG. 5

MEAN $\hat{A}_{QRS}$, $\hat{A}_T$ AND $\hat{G}$ OF 77 PATIENTS WITH LBBB



The mean A_{QRS}, A_T and G in the frontal plane projection of the 77 patients with LBBB shown in figure 4.

sÊ-loop exceeded 0.12 second. The T sÊ-loop and J had typical characteristics of LBBB or LVH, or both.

The *ventricular gradient,* $\hat{A}_{QRS}$ and $\hat{A}_T$ for the frontal plane projection for the 32 patients with LBBB associated with LVH (Fig. 7) were essentially as described for all 77 patients (Figs. 4 and 5). The mean $\hat{A}_{QRS}$ for the 32 patients with LBBB and LVH was oriented to the left and superiorly with a magnitude of 73.8 μv. s. and a direction of –27°. The mean $\hat{A}_T$ was 47.4 μv. s. in magnitude and +121° in direction. The mean $\hat{G}$ was 45.5 μv. s. in magnitude and –10° in direction (Fig. 7). These 3 vectors differed from the normal mean vectors.[12]

Comment: Except for the duration of the QRS sÊ-loop, many of the spatial vectorcardiograms of patients with LBBB associated with LVH (Fig. 6) had the same configurations as those found in LVH alone (Fig. 8). It can be seen that the QRS sÊ-loop and QRS complexes of the EKG. in figure 6 are very similar to those in figure 8, except for greater duration. Therefore, it is difficult to know if LBBB was present in patient No. 41 (Fig. 6). Although there is no doubt that LBBB will produce tracings of this type, it is necessary to realize that the electrocardiographic criteria for LBBB are somewhat arbitrary. For example, figure 9 shows progressive widening of the QRS complex in the electrocardiogram of a patient with arterial hypertension whose last EKG. and QRS sÊ-loop resembled LVH except for the duration of the QRS complex. Such difficulties need study, particularly since LBBB is so frequently associated with LVH.

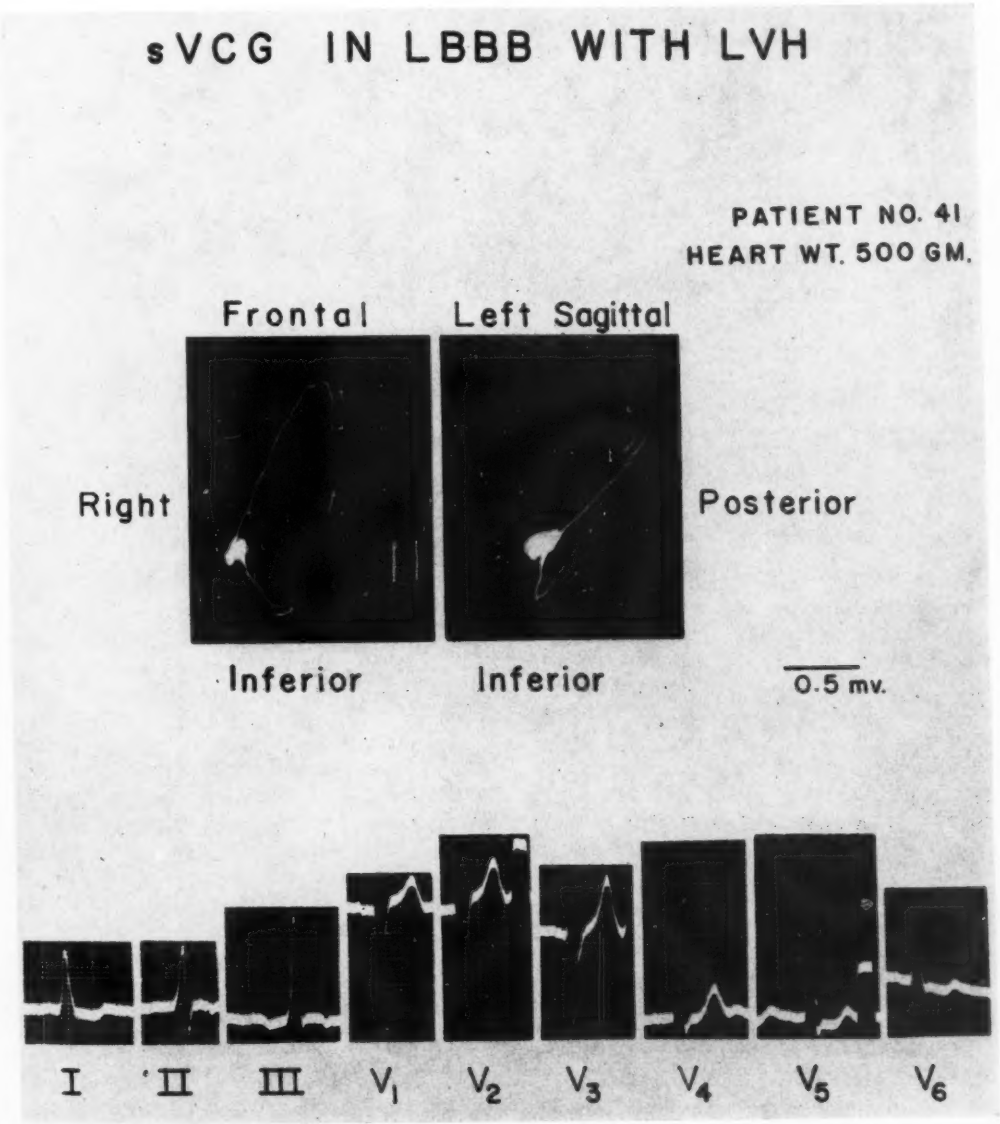
It is usually considered that patients with electrocardiograms resembling LVH but with a QRS duration of over 0.12 second have LBBB with LVH. Five of the 6 patients whose hearts showed LVH at autopsy and who had a LBBB pattern in the EKG. showed vectorcardiographic characteristics of LVH (Fig. 8). The remaining patient with LVH and LBBB

did not have the characteristic pattern of LVH in the sVCG (Fig. 10). Another patient who is still living and who had intermittent LBBB with a QRS sÊ-loop resembling LVH (Fig. 11, B) did not show evidence of LVH in the electrocardiogram during normal conduction (Fig. 11, A). Therefore, since there are both types of exceptions to the general characteristics, it is necessary to exercise caution when interpreting the sVCG of a particular patient.

Left Bundle Branch Block and Myocardial Infarction

The hearts of 15 patients with LBBB and myocardial infarction were examined at autopsy and the lesions were identified and

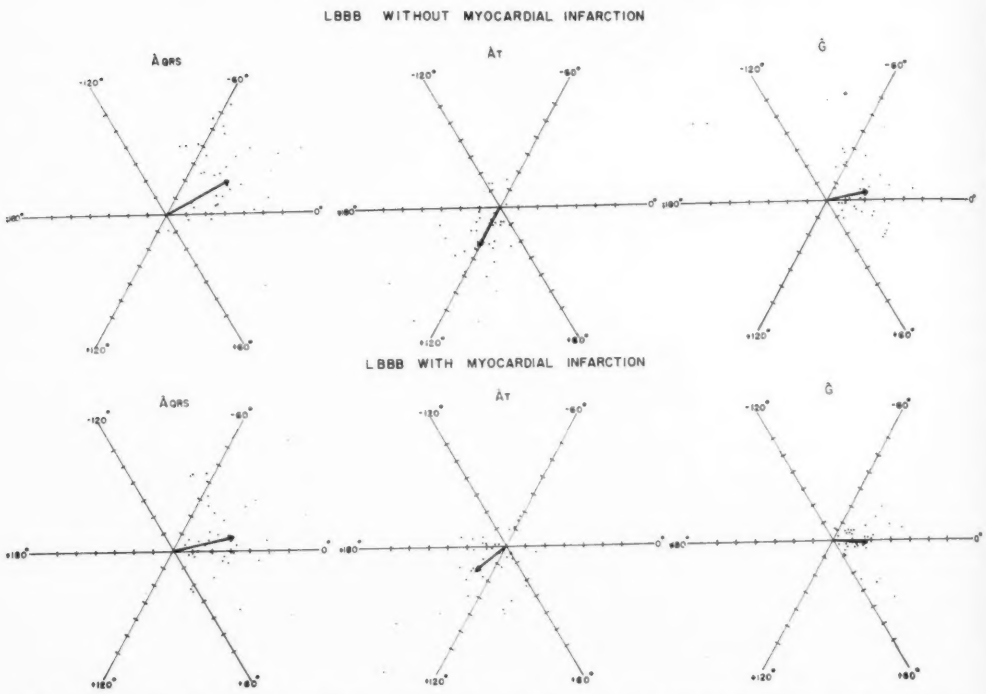
FIG. 6



The sVCG and EKG. in a patient with LBBB and LVH. The heart weighed 500 Gm. at autopsy.

FIG. 7

$\hat{A}_{QRS}$, $\hat{A}_T$, AND $\hat{G}$ IN LBBB WITH AND WITHOUT MYOCARDIAL INFARCTION



The mean (arrow) and individual (dots) magnitudes and directions of the A_{QRS}, A_T and G in the patients with LBBB with and without myocardial infarction. All patients had LVH in association with LBBB.

localized. This group constituted the most important source of data for this study. In addition, there were 20 patients who had LBBB and clinical evidence typical of myocardial infarction.

The Spatial Vectorcardiogram: Each of the 15 patients whose hearts showed infarcts at autopsy had infarcts of the anterior surface or at least of the apical portion of the heart. Five hearts had infarcts of the anterior surface only, whereas 10 had a combination of lesions. The QRS sÊ-loops of these 15 patients had the general characteristics of LBBB indicated above; all were markedly distorted and oriented posteriorly to the isopotential point. The mean instantaneous vectors of the QRS sÊ-loops which were inscribed when the areas of infarction failed to be depolarized tended to be shortened or directed away from the infarcted areas.[14] The posterior displacement was generally greatest in those patients with a strictly anterior infarct (Fig. 12), but the patients who had multiple infarcts had the most distorted QRS sÊ-loops (Fig. 13).

Of the other 9 patients (all without infarcts) whose hearts were examined at autopsy only one showed such a marked posterior displacement of the QRS sÊ-loop. However, the patient was in shock with a marked reduction in blood pressure when the recordings were obtained. It is possible that the anterior wall of the heart was not adequately perfused and depolarization did not take place anteriorly. The QRS sÊ-loop was very similar to the one shown in figure 12 in which a large anterior infarct was found at autopsy.

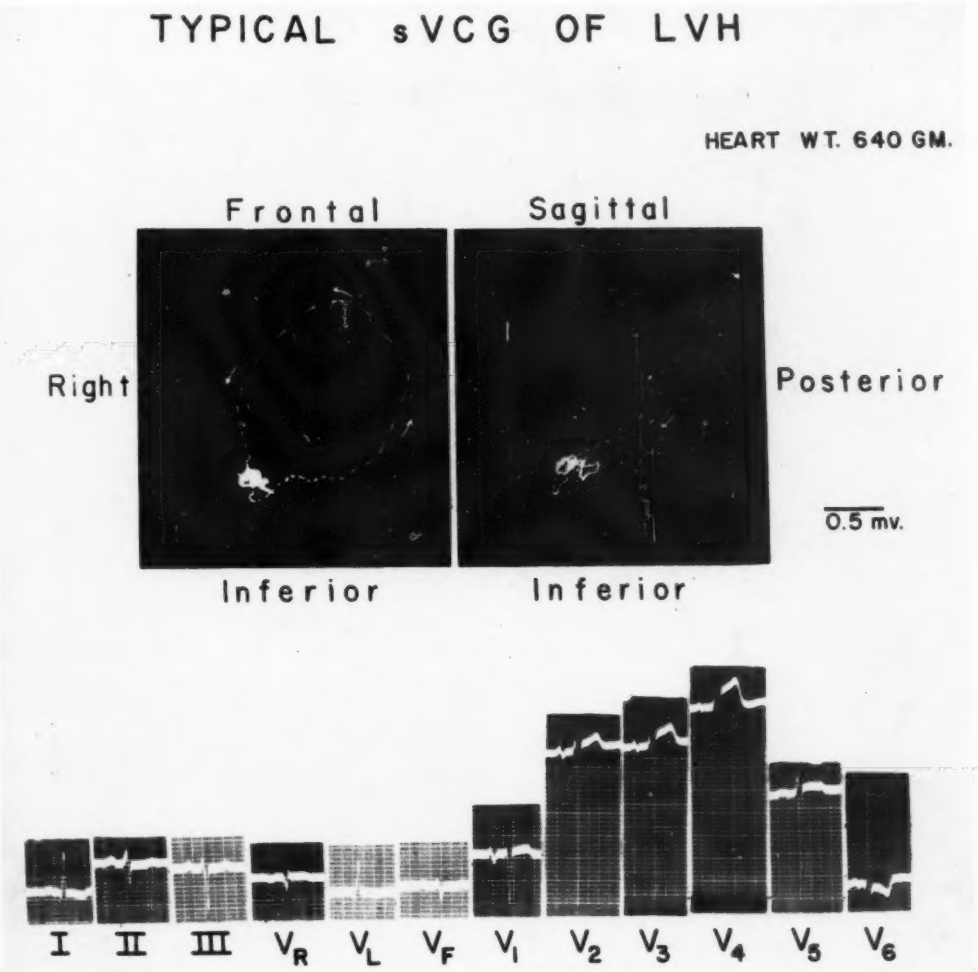
The 20 patients who had typical clinical evidence of myocardial infarction and LBBB had QRS sÊ-loops similar to those described above for the hearts which had infarcts at autopsy. Although these patients may not have had infarcts, the clinical picture was so typical of infarction in all of them that the lesions were probably present. Again, in this

group, the QRS sÊ-loops were distorted in a manner characteristic of changes that might be expected with a local loss of cardiac muscle. Marked distortions in the QRS sÊ-loop were common for the patients with infarction. These distortions were greater than those described for aging.[15]

The Ventricular Gradient: The magnitude and direction of $\hat{A}_{QRS}$, $\hat{A}_T$ and $\hat{G}$ are summarized in figure 7 which shows the effect of myocardial infarction on the ventricular gradient. The $\hat{A}_{QRS}$, $\hat{A}_T$ and $\hat{G}$ are similar to those seen in LBBB with LVH (Fig. 7), except for a slight rotation of $\hat{A}_{QRS}$ and $\hat{G}$ to the right in the former group. This downward displacement of the $\hat{A}_{QRS}$ was also seen in the QRS sÊ-loop.

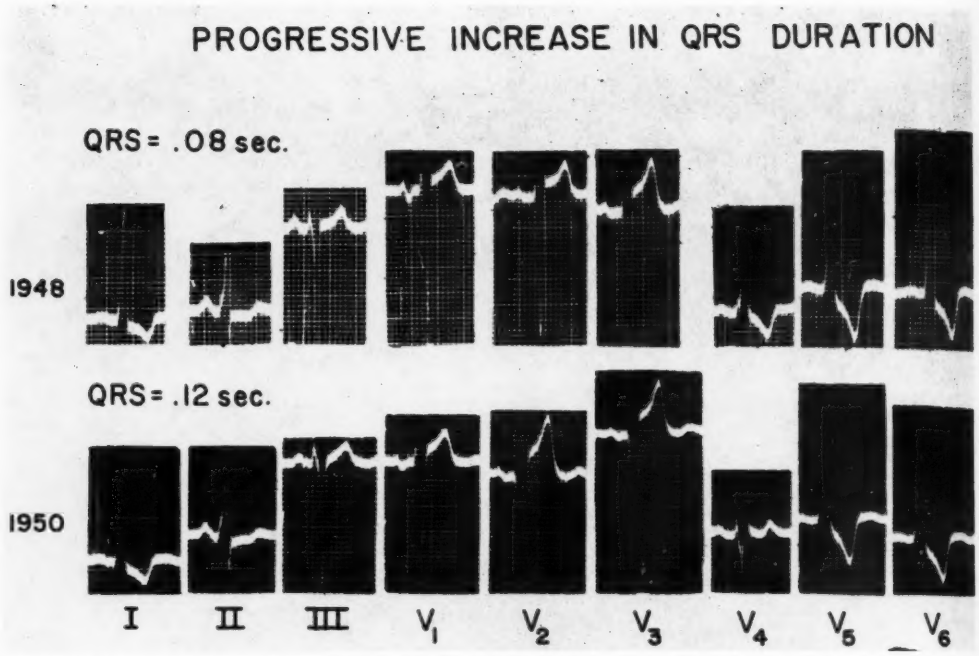
Comment: That myocardial infarction cannot be recognized in the presence of LBBB has been generally accepted because the time course of depolarization is so greatly altered in LBBB that it was thought that any further alterations produced by infarction could not be recognized. Although this may be true, it seems that the time course of depolarization proceeding from the right side

FIG. 8



A typical sVCG and EKG. of a patient with LVH without LBBB whose heart weighed 640 Gm. at autopsy.

FIG. 9



EKG. showing the progressive increase in duration of the QRS complex over a 2 year period. The latest tracing was considered to represent LBBB but probably represented LVH in which the left ventricle was so hypertrophied that it required more than 0.12 second to depolarize it. Consult text for details.

of the septum as a result of the LBBB and progressing through an essentially normal left ventricle would differ from the time course of depolarization through a left ventricle in which large masses of muscle are electrically inactive as a result of infarction (Fig. 14). The same would be true for LVH or any other lesion of the heart. Thus, if it were possible to compare in detail the time courses of depolarization in hearts with normal myocardiums and only localized lesions of the left bundle branch with the time courses of depolarization in hearts with LBBB and myocardial diseases, differences in these time courses could be recognized in spite of the presence of LBBB. Fortunately, the sVCG displays the time course of depolarization in detail so that it is only necessary to learn the differences manifested. For example, figure 15 shows a marked reduction in the magnitude of the vectors of the QRS sÊ-loop in its mid-temporal portion. This indicates a definite alteration in the time course of depolarization at that time. This change is compatible with alterations theoretically expected for an infarct of the lateral wall of the left ventricle with loss of muscle and, in turn, loss of associated electric forces. This patient had a typical clinical picture of infarction. Such a concave deformity of the QRS sÊ-loop has not been encountered in patients with LBBB who did not have evidence of an infarct.

It appears, therefore, that with continued effort it may be possible to recognize with considerable accuracy the changes in the sVCG produced by infarction in the presence of LBBB. Careful clinical and autopsy correlation will be necessary to establish the diagnostic patterns.

Left Bundle Branch Block and Diffuse Myocardial Disease

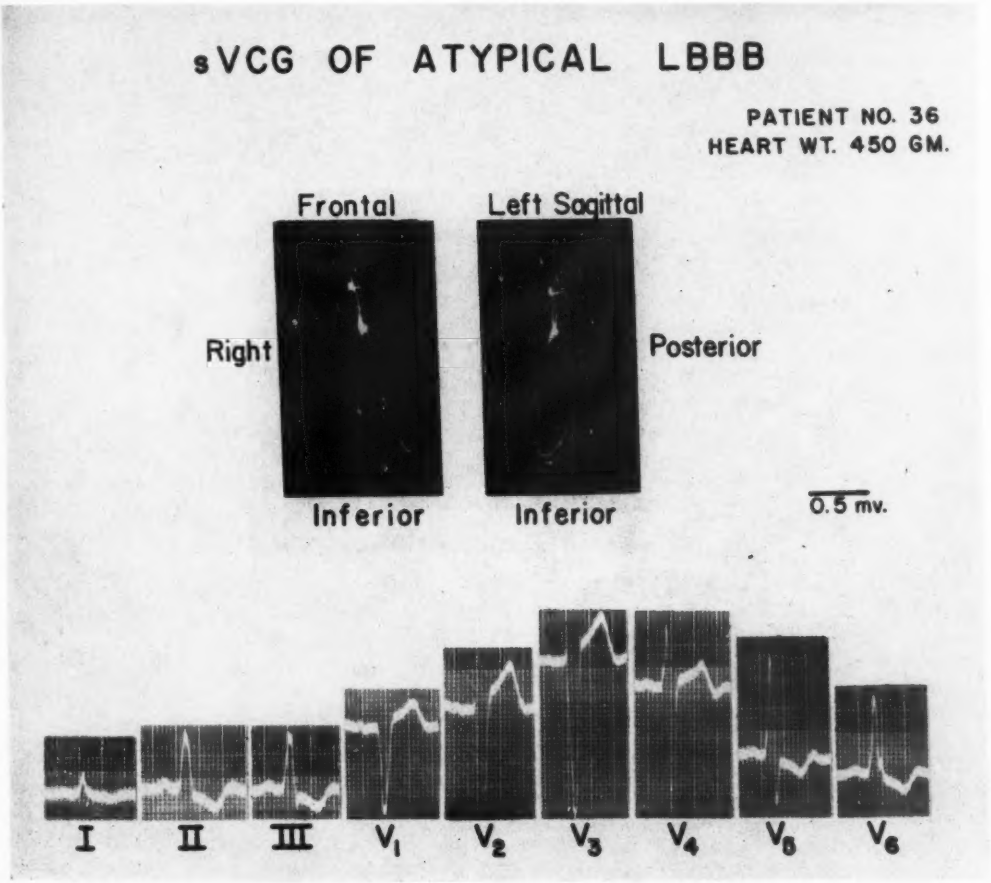
Nine of the 24 hearts with LBBB examined at autopsy showed diffuse myocardial disease. One had myocarditis and 8 had several large infarcts with diffusely scattered scars. In addition, there were 5 patients with LBBB who had diffuse myocardial disease as a result of rheumatic or idiopathic myocarditis.

The Spatial Vectorcardiogram: All 9 hearts in which diffuse myocardial disease and inflammatory or myocardial degeneration or both, were found at autopsy displayed narrow, distorted QRS sÊ-loops (Fig. 16). In addition, these loops were displaced to the left, superiorly and posteriorly. All 9 patients had had LVH. The 5 patients with clinical evidence of myocarditis had similar QRS sÊ-loops. The hearts of these patients must have been diffusely diseased but they were not examined at autopsy. Narrow, distorted loops were also found among the patients with clinical evidence of LVH and large or multiple infarcts, but, again, the hearts were not examined at autopsy. These patients had diffusely enlarged hearts with congestive heart failure and a gallop rhythm was present in many.

The Ventricular Gradient: The magnitude and direction of $\hat{A}_{QRS}$, $\hat{A}_T$ and $\hat{G}$ for the patients with rheumatic or idiopathic myocarditis were similar to those found in LBBB with LVH.

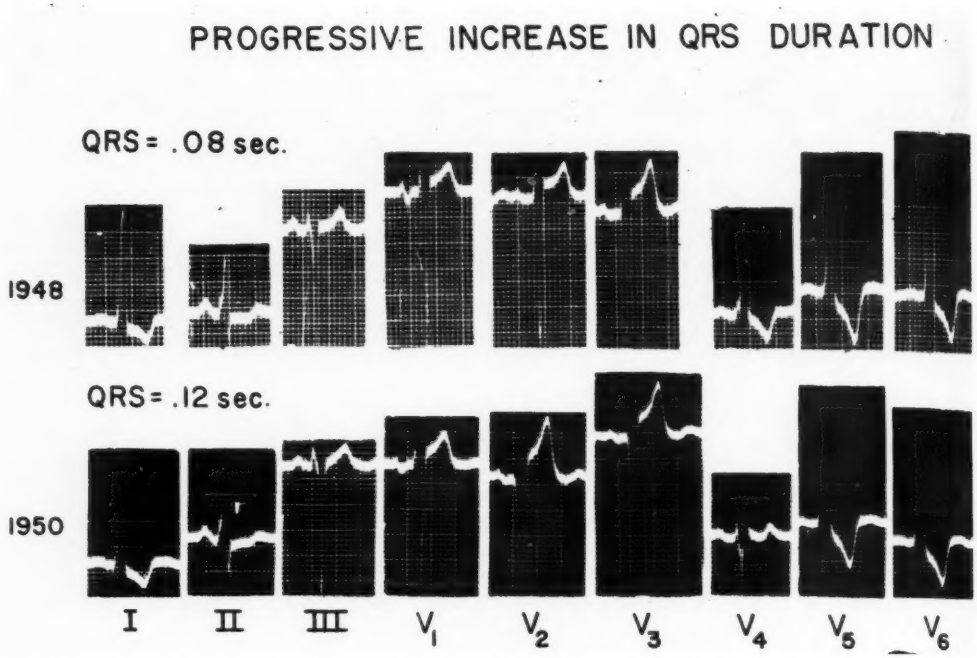
Comment: Diffuse myocardial disease in the presence of LBBB was associated with a narrow and distorted QRS sÊ-loop which was oriented superiorly, posteriorly and to the left. Since all of the patients had LVH, the spatial orientation of the QRS sÊ-loop may have been influenced by this factor; however, LBBB alone could have produced such a spatial orientation. The mechanism by which diffuse

FIG. 10



The sVCG of a patient with an atypical pattern of LBBB and LVH.

FIG. 9



EKG. showing the progressive increase in duration of the QRS complex over a 2 year period. The latest tracing was considered to represent LBBB but probably represented LVH in which the left ventricle was so hypertrophied that it required more than 0.12 second to depolarize it. Consult text for details.

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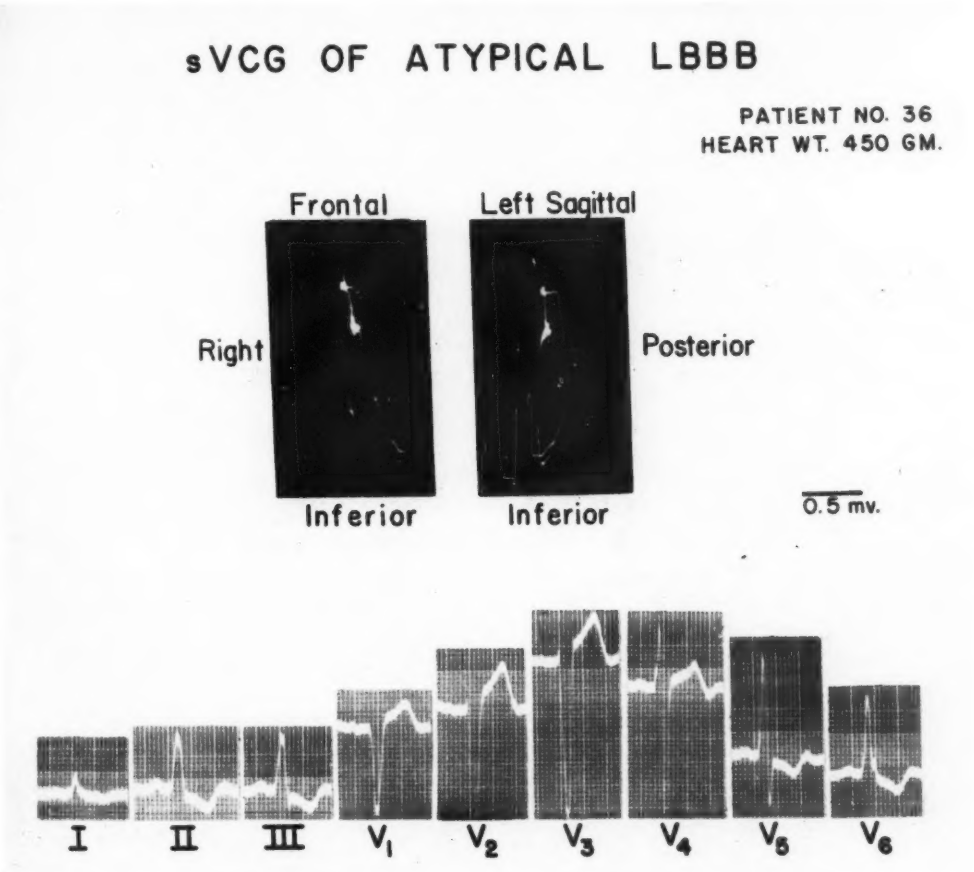
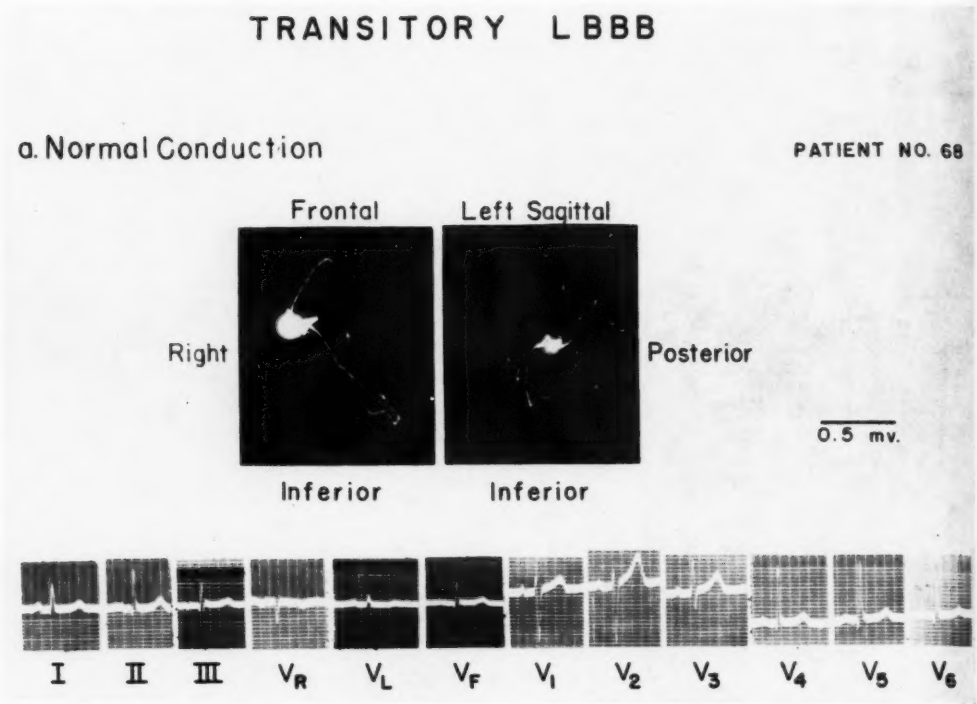
FIG. 10



The sVCG of a patient with an atypical pattern of LBBB and LVH.

FIG. 11, A



The sVCG and EKG. of a patient with transitory LBBB. (A) Shows the records for normal conduction. (Reprinted courtesy of the *American Journal of Medicine.*)

myocardial disease produces a narrow and distorted QRS sÊ-loop is not known but the relationship of this sVCG pattern to diffuse myocardial disease is so common that the configuration of the sVCG has diagnostic significance.[16]

Left Bundle Branch Block without Other Myocardial Disease

Except for complete left bundle branch block only 2 patients had hearts which were considered "normal." Seventy-five patients demonstrated either clinical or pathologic abnormalities in addition to the block. All of the hearts which were examined at autopsy were abnormal and all had myocardial hypertrophy except the 2 in which there were metastatic lesions in the myocardium. The 2 patients with only LBBB are still living. One of them had intermittent complete left bundle branch block. Figures 11, A and B show the sVCG and EKG. during normal and blocked conduction. During normal conduction the electrocardiogram and the sVCG for this patient were normal in configuration except for distortion of the QRS sÊ-loop similar to that described for aging.[15] During the LBBB the sVCG was displaced horizontally and to the left with a slow counterclockwise rotation and with slight distortion of the QRS sÊ-loop. The T sÊ-loop was displaced about 180° from the QRS sÊ-loop showing the typical configuration described above for LBBB. It is interesting to note that the Ĝ changed very little except for a slight decrease in magnitude during the LBBB, whereas $\hat{A}_{QRS}$ and $\hat{A}_T$ rotated to the left and right, respectively, and increased in magnitude (Fig. 17). This, of course, is further evidence of a normal myocardium with the disturbance localized in the left bundle branch.

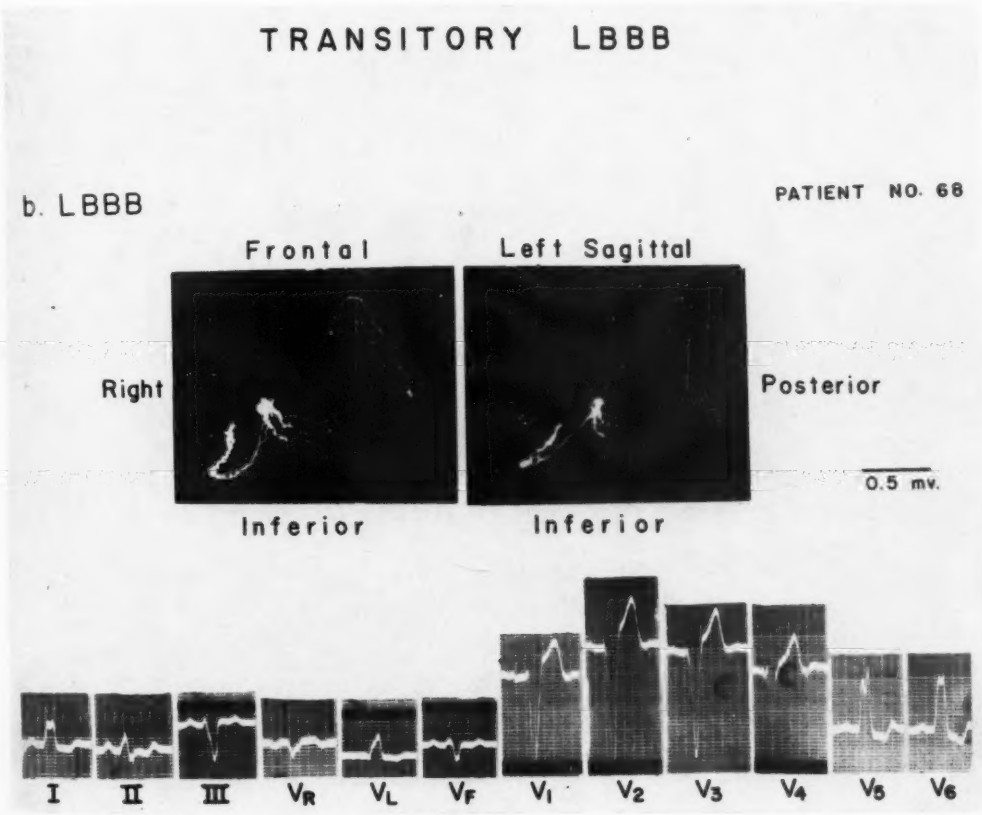
General Discussion

The recorded history of bundle branch block began as early as 1910 when Eppinger and Rothberger[17] experimentally destroyed the bundle branches. In 1945, Wilson and associates[18] pointed out that in the presence

of LBBB it is seldom possible to make the diagnosis of myocardial infarction on the basis of electrocardiographic findings alone. Since that time reports have appeared in which the diagnosis of myocardial infarction was made electrocardiographically despite the presence of LBBB. However, Chapman and Pearce[8] presented the first systematic attempt to provide criteria for the diagnosis of infarction in the presence of LBBB based on a large series of cases, some of which were studied at autopsy. These investigators considered the presence of Q waves in leads I, aV_L and V_6 as indicative of extensive anteroseptal infarction, whereas a rsR' pattern in leads I, aV_L and V_6 and a notched S wave in the precordial lead to the right of the transition zone were associated with a moderately extensive anteroseptal infarct. Anteroseptal infarction was suspected whenever the R wave failed to increase progressively in magnitude in leads V_1 through V_6. Posterior infarction was considered to be present when there was a R' or a notched R wave in lead aV_F. Septal infarction was diagnosed by an initial notching of the S wave in lead aV_F.

The ventricular gradient in LBBB has received little attention. Sodi-Pallares and associates[5] described 15 cases in which the $\vec{A}_{QRS}$ was located between −58° and +90° in the frontal plane and the $\vec{A}_T$ was generally oriented in the opposite direction. They also showed that $\vec{G}$ was shortened and that the ratio of $\vec{G}$ to $\vec{A}_{QRS}$ was less than unity. Pantridge[4] studied the ventricular gradient in 18 patients with LBBB and found $\vec{G}$ to be normal in patients with minimal heart disease and abnormal in patients with moderate to

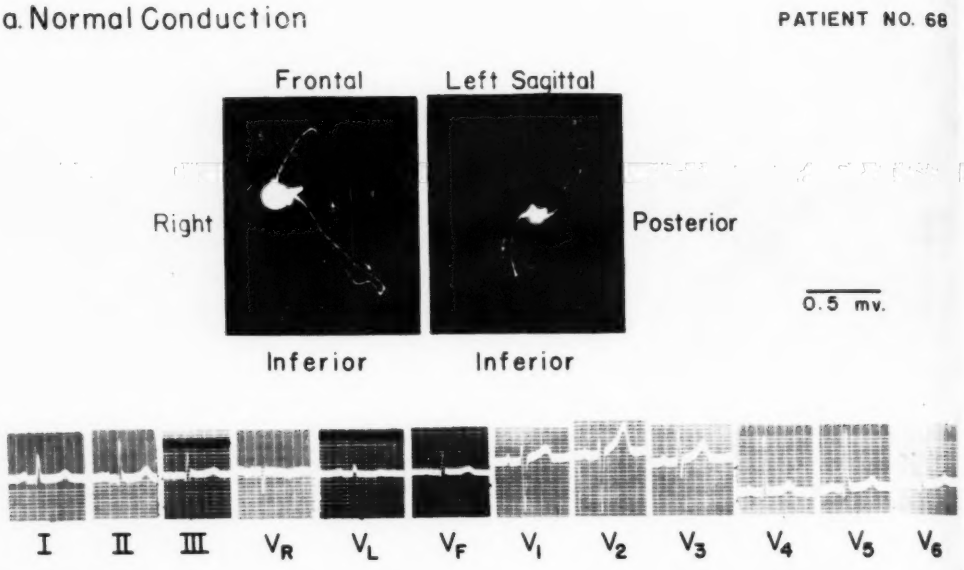
FIG. 11, B



The sVCG and EKG. of a patient with transitory LBBB. (B) Shows the records for LBBB. (Reprinted courtesy of the *American Journal of Medicine.*)

FIG. 11, A

TRANSITORY LBBB



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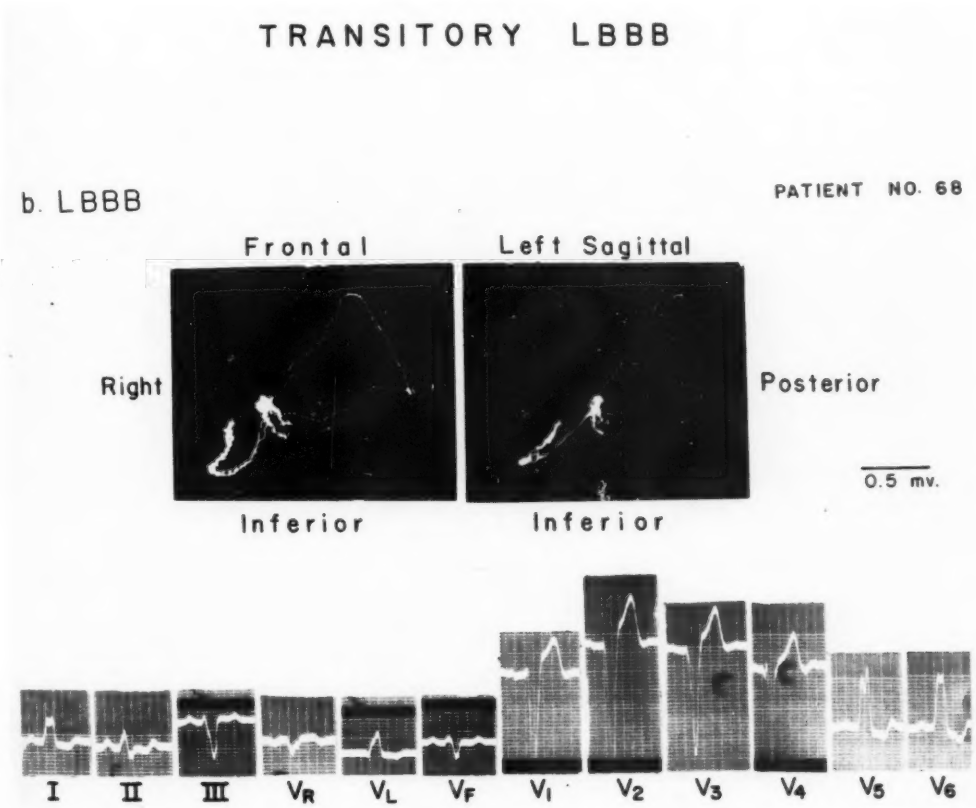
The recorded history of bundle branch block began as early as 1910 when Eppinger and Rothberger[17] experimentally destroyed the bundle branches. In 1945, Wilson and associates[18] pointed out that in the presence

of LBBB it is seldom possible to make the diagnosis of myocardial infarction on the basis of electrocardiographic findings alone. Since that time reports have appeared in which the diagnosis of myocardial infarction was made electrocardiographically despite the presence of LBBB. However, Chapman and Pearce[8] presented the first systematic attempt to provide criteria for the diagnosis of infarction in the presence of LBBB based on a large series of cases, some of which were studied at autopsy. These investigators considered the presence of Q waves in leads I, aV_L and V_6 as indicative of extensive anteroseptal infarction, whereas a rsR' pattern in leads I, aV_L and V_6 and a notched S wave in the precordial lead to the right of the transition zone were associated with a moderately extensive anteroseptal infarct. Anteroseptal infarction was suspected whenever the R wave failed to increase progressively in magnitude in leads V_1 through V_6. Posterior infarction was considered to be present when there was a R' or a notched R wave in lead aV_F. Septal infarction was diagnosed by an initial notching of the S wave in lead aV_F.

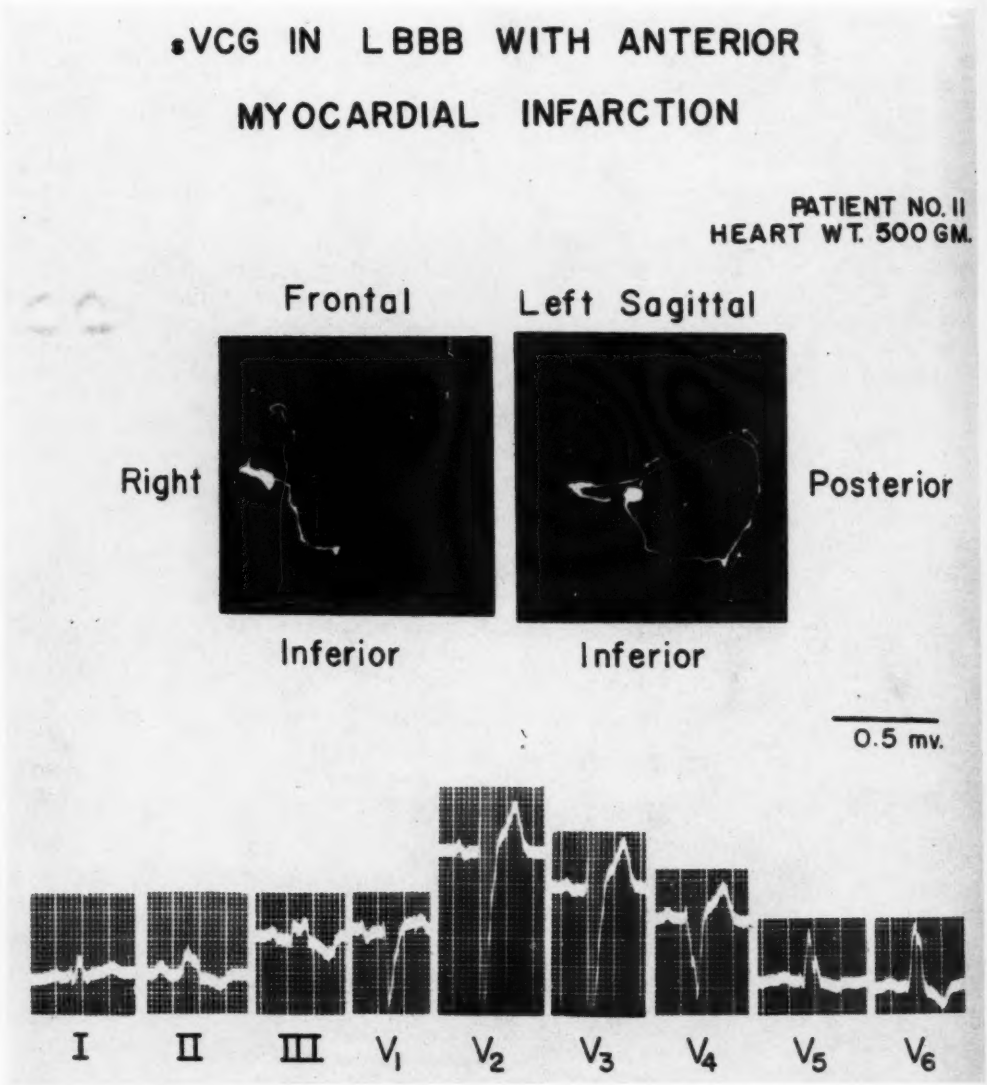
The ventricular gradient in LBBB has received little attention. Sodi-Pallares and associates[5] described 15 cases in which the $\hat{A}_{QRS}$ was located between −58° and +90° in the frontal plane and the $\hat{A}_T$ was generally oriented in the opposite direction. They also showed that $\hat{G}$ was shortened and that the ratio of $\hat{G}$ to $\hat{A}_{QRS}$ was less than unity. Pantridge[4] studied the ventricular gradient in 18 patients with LBBB and found $\hat{G}$ to be normal in patients with minimal heart disease and abnormal in patients with moderate to

FIG. 11, B



The sVCG and EKG. of a patient with transitory LBBB. (B) Shows the records for LBBB. (Reprinted courtesy of the *American Journal of Medicine.*)

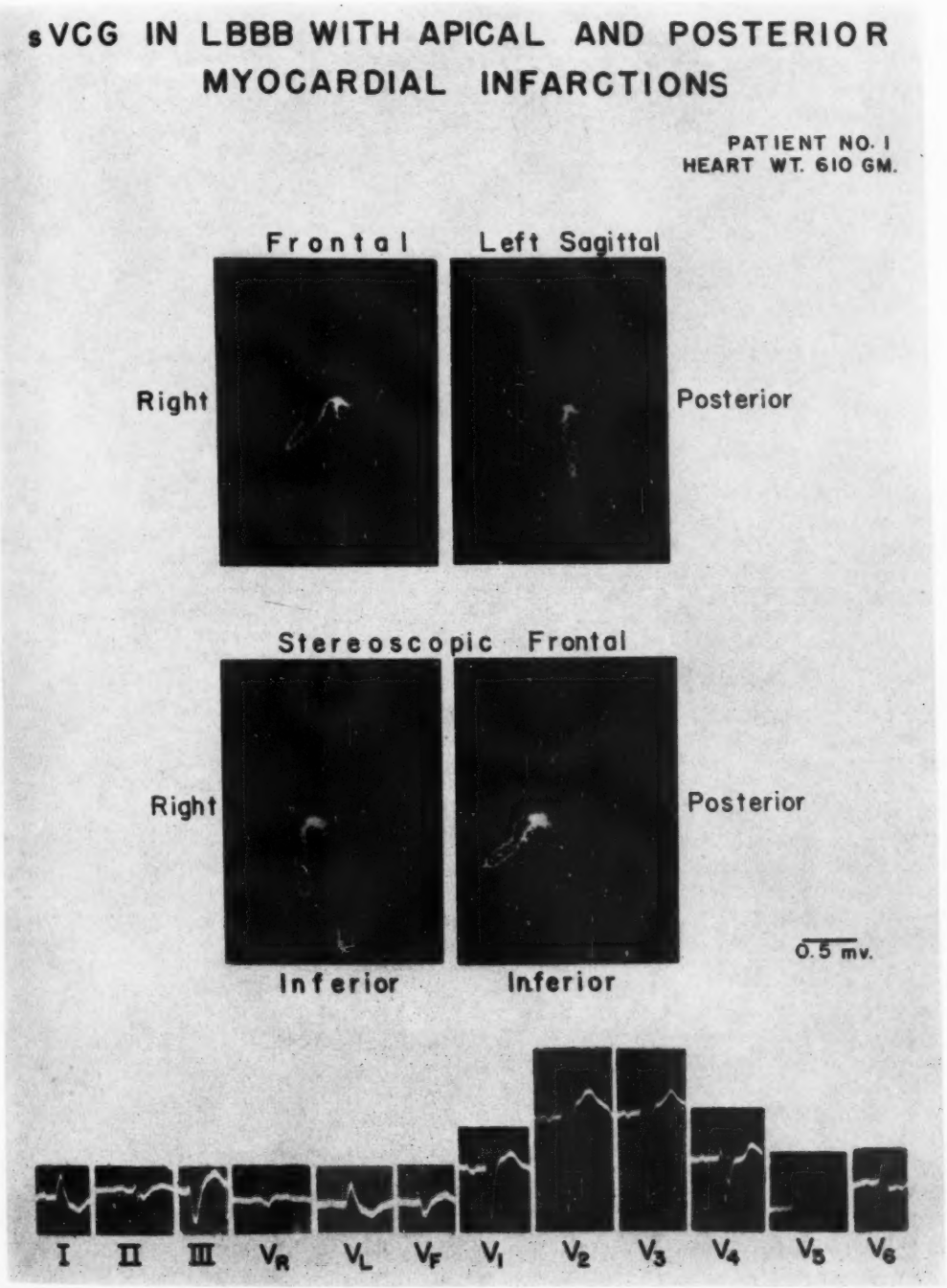
FIG. 12



The sVCG of a patient with LBBB, LVH and an anterior myocardial infarct. Note the marked posterior displacement of the QRS sE-loop, an uncommon orientation for LBBB except with anterior infarction.

severe heart disease. He found the ratio of $\hat{G}$:$\hat{A}_{QRS}$ to be less than 1.0 even in patients who had not received digitalis. After studying 32 cases of LBBB, Mezzasalma and Moschini[6] concluded that the $\hat{A}_{QRS}$ was usually in the first sextant of the triaxial reference system, while the $\hat{A}_T$ was usually located in the fourth sextant. $\hat{G}$ was usually between 0° to 90°. Caccuri and Graziani[7] examined the gradients in 40 patients with LBBB between the ages of 29 and 75 years and found the $\hat{A}_{QRS}$ to be between −76° and +54° with 32 of the 40 vectors being in the first and second sextants of the triaxial system and the remainder in the sixth sextant. The magnitude of $\hat{A}_{QRS}$ was 19 to 308 μv. s. The $\hat{A}_T$ was directed between −161° and +176° in the frontal plane with a magnitude of 4 to 228 μv. s., whereas $\hat{G}$ was

FIG. 13



The sVCG of a patient with LBBB, LVH and posterior and apical myocardial infarctions. Note the marked distortion of the QRS sE-loop and the superior orientation of the early portion of the loop. The diffuse myocardial disease has resulted in a narrow QRS sE-loop.

FIG. 12

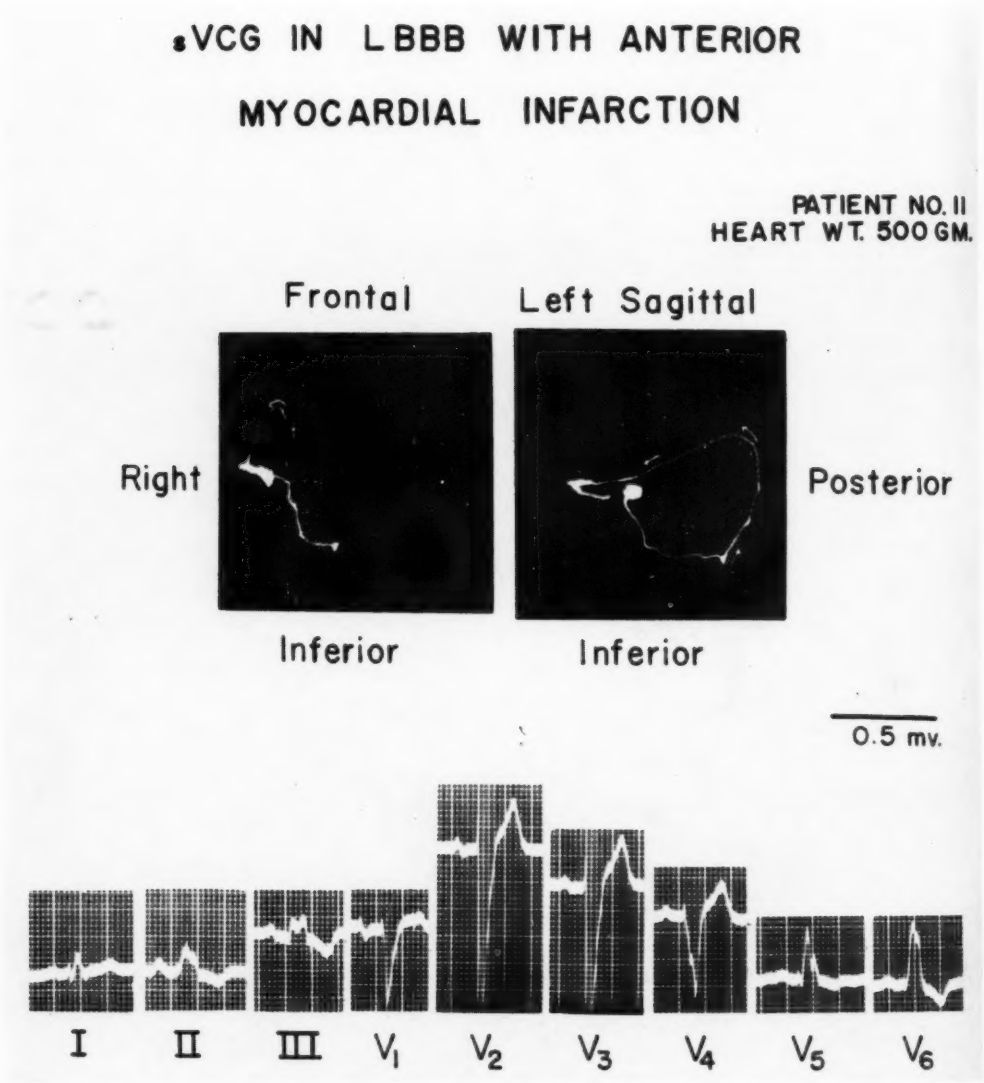


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FIG. 13

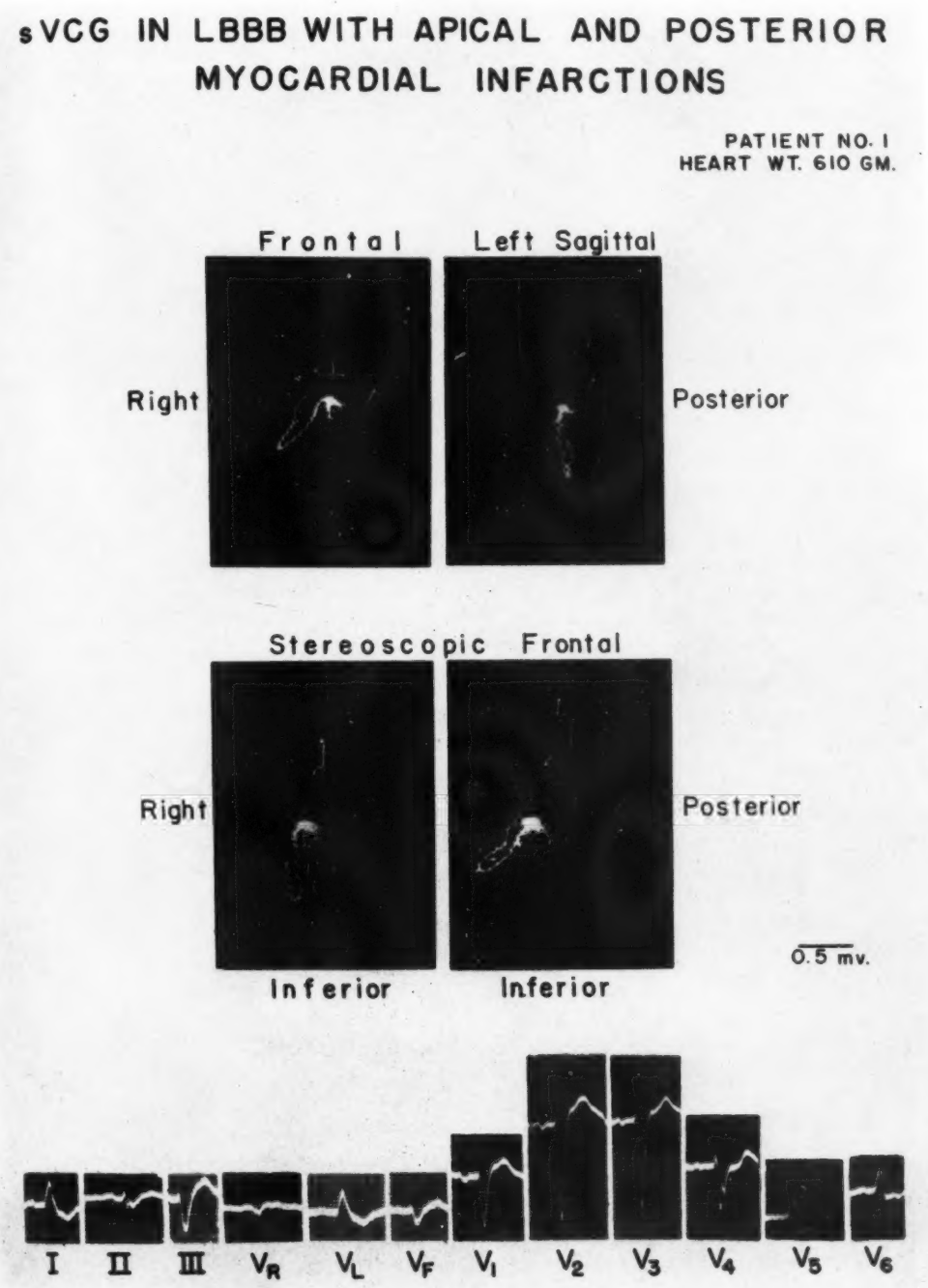

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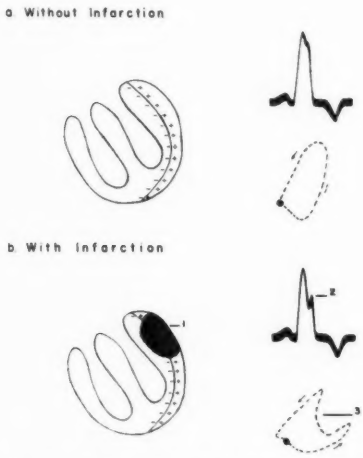
FIG. 14

INFLUENCE OF INFARCTION ON THE sVCG IN LBBB



A schematic representation of how an infarct of the left ventricle might produce an alteration of the QRS sÊ-loop in spite of LBBB. (A) Shows the depolarization process migrating from the right through the wall of the left ventricle in the absence of infarction. (B) Shows the same process migrating through the wall of a left ventricle with an infarct. In the latter instance the time course of depolarization is altered. Possible resultant QRS sÊ-loops are shown. The temporal factor must be considered when attempting to identify and localize infarcts from the sVCG. (Reprinted courtesy of the *American Journal of Medicine.*)

between –96° and +97° in the frontal plane projection with a magnitude of 16 to 292 μv. s. These authors were of the opinion that the gradient was normal in most cases and could find no relationship between the ventricular gradient and the existence of myocardial disease.

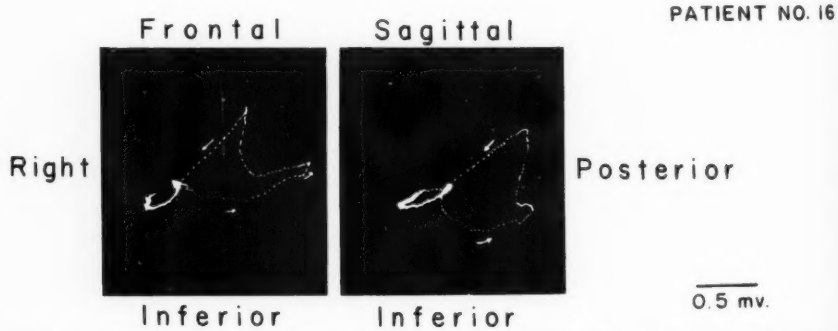
Although the spatial vectorcardiogram in LBBB has been described previously,[1-3] reports dealing with the vectorcardiogram in LBBB complicated by myocardial infarction are rare. Deglaude and Laurens[19] described 2 patients with autopsy studies in which they considered the vectorcardiograms diagnostic of myocardial infarction. These observations were based primarily on distortions in the QRS sÊ-loops. Wenger and Hupka[20] considered the most important change in the sVCG in posterior myocardial infarction as an initial anterior displacement of the QRS sÊ-loop followed by an abrupt posterior displacement.

In this investigation the hearts of 24 patients, approximately one third of the patients studied, were examined at autopsy, making it possible to evaluate the relationship of the vectorcardiograms and ventricular gradients to the complicating cardiac lesions. Unfortunately, serial sections of the hearts were not obtained and so the lesions in the left bundle branch itself could not be identified precisely.

It appears that the presence of complete left bundle branch block does not always eliminate the possibility of recognizing in the vectorcardiogram and the electrocardiogram complicating myocardial lesions. This is verified by the characteristic differences found in the configurations of the QRS sÊ-loops of 77 patients with LBBB. If the processes of depolarization and probably repolarization were recorded in sufficient detail, different diseased states could be ultimately recognized despite the existence of the block. The find-

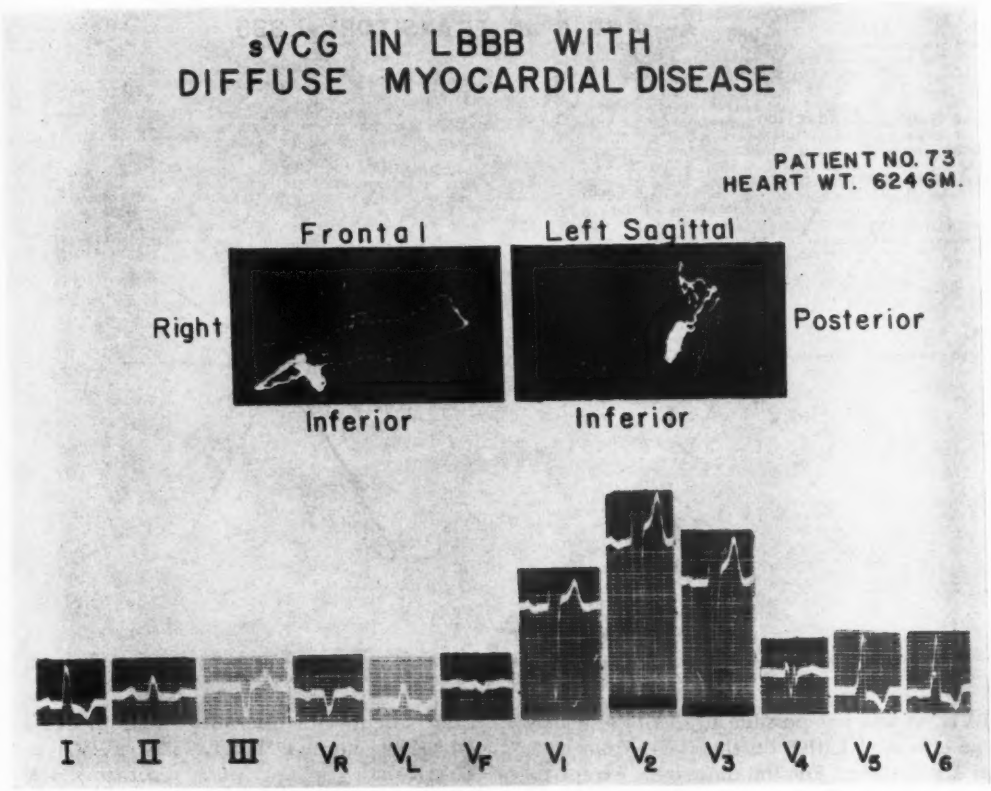
FIG. 15

sVCG IN LBBB WITH PROBABLE LATERAL INFARCTION



The sVCG of a patient with LBBB and classical clinical evidence of myocardial infarction. The marked concave deformity of the midtemporal portion of the QRS sÊ-loop is compatible with an infarct of the lateral wall of the left ventricle.

FIG. 16



The sVCG of a patient with LBBB and diffuse myocardial disease due to repeated episodes of myocarditis of rheumatic fever. The heart was hypertrophied and dilated.

ings of this investigation certainly indicate such a possibility. The QRS s$\vec{E}$-loop of the sVCG is recorded in such detail that differences in the loops of many patients with LVH with and without myocardial infarction or diffuse myocardial disease can be recognized.

The T s$\vec{E}$-loops were of little assistance in differential diagnosis because of the inability to record them in sufficient detail.

Summary

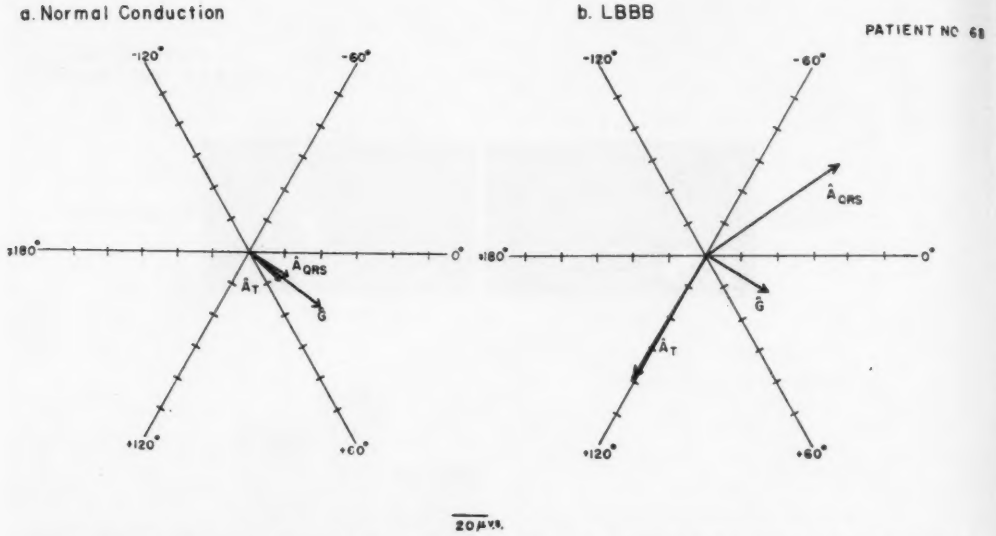
The sVCG employing the tetrahedral reference system, and the $\hat{A}_{QRS}$, $\hat{A}_T$ and $\hat{G}$ were described for 77 patients with left bundle branch block. The hearts of approximately one third of these patients were studied at autopsy.

The general manifestations of LBBB in the sVCG and the ventricular gradient were described. These included a QRS s$\vec{E}$-loop which was inscribed slowly in a counterclockwise direction and which was oriented to the left, superior and slightly posterior to the isopotential point. The T s$\vec{E}$-loop was generally oriented 180° away from the QRS s$\vec{E}$-loop and began from J which was spatially oriented to the right, inferior and anterior to the isopotential point. The $\hat{A}_{QRS}$ was located to the left and superiorly in the frontal plane projection with the mean vector being in the first sextant of the triaxial reference system, whereas $\hat{A}_T$ was to the right and inferiorly with the mean vector in the fourth sextant. The ventricular gradient was to the left and slightly inferior and was of normal magnitude. Although $\hat{G}$ was normal in magnitude and direction, it was relatively small with respect to $\hat{A}_{QRS}$, the $\hat{G}$:$\hat{A}_{QRS}$ ratio being less than unity (mean, 0.64).

Since most of the patients with LBBB had

FIG. 17

$\hat{A}_{QRS}$, $\hat{A}_T$, AND $\hat{G}$ IN TRANSITORY LBBB



A_{QRS}, A_T and G for the frontal plane projection of the patient with transitory LBBB during normal conduction (A), and during the LBBB (B). Note the relatively small change in G with the change in conduction.

LVH, it was not possible to distinguish fully the effects of LBBB on the sVCG from those of LVH alone. For the most part, except for the slower inscription of the QRS sÊ-loop, the sVCG in LBBB with LVH was similar to that seen in LVH alone. The ventricular gradient in LBBB with LVH was similar to that which was described for all of the patients.

When LBBB was complicated by myocardial infarction, the QRS sÊ-loop was markedly distorted. Theoretical considerations have been presented to explain these distortions. In spite of this distortion in the QRS sÊ-loop the general characteristics of LBBB were retained in most of the sVCG. The $\hat{A}_{QRS}$, $\hat{G}$ and QRS sÊ-loop were not deviated as far to the left in LBBB with LVH and myocardial infarction as in LBBB and LVH without myocardial infarction.

The sVCG in LBBB with diffuse myocardial disease presented the same characteristics as previously described from this laboratory. The most outstanding feature was the narrow QRS sÊ-loop.

An interesting observation was the sVCG in a patient with intermittent LBBB and an otherwise normal heart. The sVCG and ventricular gradient were recorded during normal conduction and during the LBBB and $\hat{G}$ remained unchanged. This showed the effects of LBBB itself on these parameters.

There is a need for further study of the electrocardiogram and vectorcardiogram in myocardial infarction with LBBB to evaluate and improve the accuracy of the diagnosis of complicating cardiac lesions in the presence of LBBB. Greater emphasis should be given to autopsy correlations.

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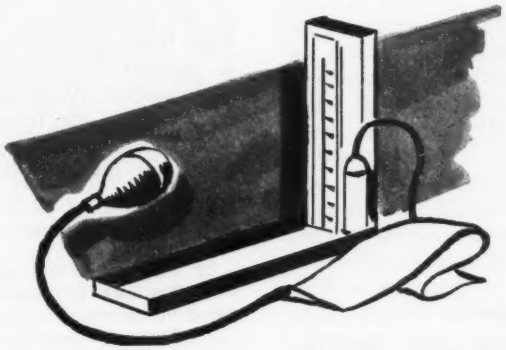

A Review of the "Fibrositis" Question*

CARL W. LAFRATTA, M.D., and JACK B. PORTERFIELD, M.D.,†
Kecoughtan, Va.

Pain referred to the muscles is one of the very common complaints of everyday practice. Yet little is known of the lesion or its cause. The authors consider the present state of confusion and attempt to bring some degree of order to the problem for both understanding and symptomatic treatment.

THERE SEEMS TO BE NO DOUBT that, when the term "fibrositis" is used either in a round table discussion or in the literature, the concepts so entertained by the listeners or the readers are quite varied. We are struck by the confusion and lack of consistency with respect to the description of this disease entity. It is significant that many terms have been accumulated over the years in denoting this condition. The following have been used at one time or the other:

Fibrositis
Myalgia
Myositis
Myofascitis
Myofascitic syndrome
Fibromyositis
Myofibrositis
Fascitis
Myogelosis
Muscular rheumatism
Fibropathic syndrome
Muscular strain
Nonarticular rheumatism
Myofascial pain syndrome
Psychogenic rheumatism

Definition

The most popular term in the literature still seems to be "fibrositis," a term introduced by Sir William Gowers in 1904 in an article on lumbago. Stockman in 1920 apparently was the first to describe what was believed to be the underlying pathologic change, namely, "a condition of chronic inflammation of white fibrous tissue of the fascial aponeuroses, sheaths, muscles and nerves, ligaments, tendons, periosteum and subcutaneous tissues, occurring in all parts of the body, giving rise to pain, aching, stiffness and other symptoms, the result of preceding general infections or local inflammations or injuries." For a time this very plausible theory was grasped by frustrated physicians seeking a cause for the manifold aches and pains in soft tissue structures, but subsequent studies have failed to confirm his histologic findings which suggested the presence of chronic inflammation.

Since then it has emerged as a most controversial and confused condition in the field of rheumatology, and a review of the literature reveals an unusual number of authors vehemently defending a variety of theories in regard to the pathogenesis, but in all instances the basic histologic studies of soft tissue necessary to support these theses are conspicuous by their absence. As an example of the inconsistency seen in the terminology and classification, the following types of so-called "fibrositis" are outlined in Comroe's text, "Arthritis":[1]

(1) Intramuscular (known as myositis or muscular rheumatism)
(2) Periarticular (involvement of the joint capsule)
(3) Tendinous or fascial (involvement of the fibrous sheath of tendons)
(4) Bursal (commonly called "bursitis")
(5) Perineural
(6) Panniculitis

Such classifications are, in our opinion, most confusing, incorrect and outdated, and we believe, for example, that the term "fibrositis" should not be synonomous with bursitis or synovitis since these now represent specific and distinct disease entities.

Hence, the reason we will limit this discussion today to "intramuscular fibrositis," so-called, better designated as *myofascial pain syndromes,* and as the name implies, the pain and discomfort in such instances is primarily myogenic. We believe we can readily and properly exclude other fairly well-defined entities from this group and limit the discussion

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†From the Department of Physical Medicine and Rehabilitation, VA Center, Kecoughtan, Va.

to syndromes of localized painful and tender areas in muscle, at times possibly in a tendon and the contiguous fascia, which has already been classified elsewhere as "primary intramuscular fibrositis." In other words, this syndrome would be unaccompanied by, and independent of, any other recognized disease.

The problem of terminology presents itself. We have tried in vain to find a suitable name for this entity, but frankly admit we have met with no satisfaction. The ones that seem to be most suitable at this time are "myofascitis" or the "myofascial pain syndrome," if we desire the most descriptive terms at our disposal. Throughout the rest of this discussion we will, for the most part, refer to this condition by one of these terms.

Symptomatology

The commoner sites of myofascitis are the neck, shoulder and scapular areas, lower back, gluteal region and the chest wall. The shoulder area is perhaps the commonest site. Sola[2] found so-called trigger points of myofascitis in 200 subjects commonest (in 84.7%) in the trapezius, levator scapula, infraspinatus, and scalenus in that order. Next in order were sites in the rhomboids, supraspinatus, teres major and minor. Though such locations of myofascitis are rather common, it must be emphasized that almost any skeletal muscle of the body can be the site of such involvement. Recently, we have seen involvement of the abdominal wall (also cited by Wilson[3]) and another instance referred to as the "adductor longus syndrome" by Travell.[4]

Clinically, the myofascial pain syndrome is characterized by pain and stiffness in a muscle or muscle group, usually with muscle spasm; the pain is particularly marked on movement and may be so intense the patient will not move the part. It may have an acute, subacute or chronic course with remissions and exacerbations, the patient being relatively free for days at a time. In the cases brought to our attention, it has usually been continuous. The pain may be sharp or dull, occasionally knife-like, or not uncommonly burning like a hot poker. In some instances it is a dull ache, more marked in the morning, the pain decreasing and stiffness lessening as the part is exercised. Symptoms are often precipitated by cold, damp, drafts and sudden changes in temperature, or by an unusual strain or exertion. Relief is usually obtained by heat, mild activity and even alcohol! No constitutional symptoms are found, and physical examination is notoriously negative except for the local painful disturbance. Palpation may disclose a localized tender area, the so-called "trigger area." In many cases nodules or cord-like areas can be felt in the muscle. The question then arises, "Are these areas responsible for the patient's symptoms?" Certain tests seem to indicate a direct relationship: (1) pressure over these areas may produce pain, not only locally, but in the area of referred pain; (2) pain may be produced by increasing tension in the suspected structure by stretching movements; and (3) injection of the area with a local anesthetic may bring complete relief, a full range of painless movement being restored.

The interesting and somewhat confusing fact is that such nodules are found often in persons who are not suffering pain and who give no history of myofascial pain. In 500 soldiers, Copeman and Pugh[5] found nontender nodules with equal frequency in those with and those without the diagnosis of myofascitis, but tender nodules or trigger points were found in only 3% who did not give a history of discomfort and in 30% of those who did. In our opinion the presence of nodules is not necessarily required for making such a diagnosis. Tenderness, usually exquisite, with spasm and limitation of motion, may exist without nodules.

As has been mentioned, the patient's symptoms may be limited to certain well-defined areas. The common stiff neck often associated with occipital headache has been called "cervical myofascitis." In the lumbar area a common form of myofascitis used to be called "lumbago" and constitutes one of the commoner causes, if not the commonest cause, of back pain. Gluteal involvement may be confused with the lumbar disk syndrome. In some cases of vague sciatic type of pain, examination may reveal trigger areas in the gluteal muscles which, on pressure, produce pain in the thighs, but the pain lacks the segmental distribution of a root lesion and neurologic signs of sciatic neuropathy are absent. It should be stressed that although the prominent clinical finding in this syndrome is tenderness, the patient's pain and tenderness may be referred and the site of the local trigger area may be quite apart from the area in which the pain is experienced. For example, pain in the shoulder girdle is often referred

from a trigger area. Kelly[6] found a supraspinatus trigger point in 62 of 105 cases, and pressure on these points reproduced the pain not only locally but in referred areas down the arm and into the neck. At times the actual trigger area may be unknown to the patient and a careful search may be necessary to reveal this focal point. Trite as it may sound, it behooves us to always think in terms of this syndrome when confronted by a suggestive symptomatology. We believe this disease entity is much more prevalent than is accepted by some.

Diagnosis and Differential Diagnoses

Exclusion plays a very important part in the diagnosis. This is to be stressed. Deeper seated disease of internal structures, of course, needs be taken into consideration. Rheumatoid and degenerative arthritis may be confused at times, but careful study should exclude these in just about all of the cases. Involvement of musculature of the chest wall may simulate anginal pain and can closely simulate pleuritic pain when intercostal muscles are affected (pleurodynia).

Disk syndromes in a few instances may be hard to differentiate, as mentioned above, but if typical symptoms and signs are present, pain with sciatic distribution with or without neurologic signs, ought not be confused. The shoulder-hand syndrome may begin with stiffness and pain in the fingers and shoulder, but the swelling of the hand, trophic changes, and palmar fascial changes should serve to distinguish it.

There is the question of the differentiation from cervical arthritis when dealing with neck, shoulder and arm pain. We now seem to be living in a "cervical arthritis age," and in our opinion this diagnosis is often "overplayed." Just because there is evidence of degenerative arthritic change in films of the cervical spine does not necessarily mean the patient's symptoms are due to cervical arthritis, though we will be the first to admit that when the clinical syndrome of cervical arthritis is characteristic the symptoms very often seem to outweigh the x-ray evidence. The point is that we should recognize that, even in the face of x-ray changes in the cervical spine, we may be dealing primarily with a myofascial pain syndrome. Attention is called to what Michele and his associates[7] have recently described as the "scapulocostal syndrome," a pain pattern involving the shoulder and pectoral girdle with a trigger point at the superior medial angle of the scapula with deep-seated pain in the shoulder and a spread to one or more of the following regions: (1) up the neck to the occiput and side of the head; (2) down the back of the arm and often to the forearm, wrist and hand; (3) around the chest, particularly along the course of the 4th and 5th intercostal nerves, and (4) a combination of these. The "infraspinatus syndrome," characterized by a trigger point in the inferior lateral portion of the muscle and by pain referred to the anterior lateral aspect of the shoulder and the region of the long head of the biceps, is another example of the myofascial pain syndrome which might be confusing. Time will not permit going into other trigger and reference pain areas in the various parts of the body, but there are many classical ones which have been described by Travell and Rinzler.[8]

Etiology

Much confusion and indefiniteness exist about the possible cause. Bonica,[9] writing on the subject, states "that the most important causes of myofascial pain syndromes are sudden traumas to myofascial structures." He then cites the trauma of slight injuries and as he calls them, "the microtraumas of daily living and chronic muscular strain," especially in sedentary individuals over 35. He further says that chilling, general fatigue, chronic infection and psychogenic stress may act as predisposing factors. Wallace Graham,[1] writing in Comroe's Text on Arthritis, makes the statement that no single etiologic factor has been established. He does not believe septic foci play a part. He entertains trauma as a possible factor and has no doubts about exposure to cold and the like. In a discussion of etiology there remains no doubt in the mind of the experienced observer that the symptom complex of myofascial pain syndromes may be initiated or profoundly affected in some cases by the emotional state of the individual. The observant physician cannot help but be impressed by the rather high percentage of patients with this syndrome who show evidence of a tension state.

There have been quite a few studies relative to the psychogenic factors present or not present in this syndrome, and on what is generally included in the diagnosis of myofascitis. In studies by Weiss,[10] Walters, Slade and

Graham,[11] and Ellman and Shaw,[12] it seemed definite that all found a psychopathologic accompaniment. These authors conclude that no sharp line can be drawn between so-called psychogenic rheumatism and the myofascial pain syndrome. In our opinion they *can be* differentiated in most cases. In other words, we believe psychogenic rheumatism and the myofascial pain syndrome are two different mechanisms. At the same time, we think psychogenic factors are operating in the myofascial pain syndrome in a significant number of cases. The exact role, however, is not yet universally agreed upon. Moreover, as Neufeld[13] has so aptly put it, "co-incidence of somatic symptoms and of emotional disturbances is no proof of the psychogenic origin of the symptoms, even in the absence of demonstrable organic pathology."

Copeman and Ackerman,[14,15] in 1944 and again in 1947, reported a series of biopsies performed on patients suffering from so-called "fibrositis" in which they excised the nodules from the trigger areas. In all their cases they were able to demonstrate subfascial protrusions of fat either bulging under the fascia, protruding through it, or actually peduculated through foramina. These findings were constantly in areas long associated with such syndromes and they speak of the "basic fat pattern" to be found in these areas. From their work it would appear that the "fibrositic nodule," so-called, in many instances, is in fact a fatty mass which can be broken down by sufficient trauma, such as by deep hand massage. We are in agreement to the extent that herniated fascial fat and the associated syndrome is common enough to be looked upon as a distinct entity. But should it be classified as myofascitis? Or, can it be? We, incidentally, at the Kecoughtan VA Center, have had three such patients operated upon in the past six months with complete relief of symptoms following removal of the fatty nodule.

Pathology

Graham,[1] writing in Comroe's text on arthritis, begins his discussion of the pathology with the statement that "pathological studies have not as yet revealed the fundamental nature of the disease. There is no typical microscopic appearance of the fibrositic nodule whereby it can be identified histologically; biopsies have been performed in large numbers but the pathological picture remains vague and ill-defined." All the theories as to the nature of the pathology still await histologic confirmation. In scanning the literature we can form no definite conclusions about the actual pathologic lesion since there is so much disagreement and lack of real conclusive evidence. An interesting work is that of Brendstrup, Jesperson, and Asboe-Hansen[16] who examined biopsy specimens from 12 patients having fibrositic nodules in the sacrospinalis region and compared the findings with those of a similar number of control cases. Microscopic examination disclosed a metachromatic substance in the interfibrillar connective tissue indicating acid mucopolysacchride; edema was also noticed; in a few, increased nuclei were present in muscle; and in some there was an increase in mast cells, lymphocytes and polys in the connective tissue. Chemical analysis indicated an increased fluid content and increased chloride and hexosamine concentrations in the fibrositic group. Potassium concentration was found to be lower on an average by 5 per cent. It certainly appears that more similar studies should be done whenever possible and practicable to throw more light upon this question.

Treatment

In our experience there should be some variation in the treatment program dependent upon the type of clinical picture presented. For example, an acute back condition without nodules, a trigger and reference zone, requires a somewhat different approach to treatment than in cases of a more subacute or chronic nature.

(1) *Heat.* Probably the most valuable therapeutic agent we have to treat myofascial pain is heat in some form. We, even in the field of physical medicine, seem to forget at times that the chief reason we use the various heat modalities is primarily to relieve pain. In addition, as we all know, heat relieves muscle spasm. We personally prefer to use conductive heat in the form of hydrocollator packs. These are applied to the affected part for 20 minutes to half an hour, preferably two to three times per day, and oftener at times. Infrared radiation is our second choice.

(2) *Massage.* Following heat, massage of a stroking type is used. In many clinics the massage moves beyond the moderate type, and a rather deep massage combining stroking with kneading and especially deep friction, the lat-

ter particularly over nodulation, are all used. We doubt the efficacy and even the rationale of such vigorous massage.

(3) *Rest.* This advised whenever indicated. In the acute cases rest may be very important. Its indications vary in this syndrome.

(4) *Drugs.* (a) Salicylates and other analgesic medications are used, varying according to the degree of pain being experienced.

(b) Methocarbamol (Robaxin) may be given intravenously for the relief of spasm and accompanying pain. We have had some good response to this drug and find that our best results come from intravenous administration. We do not hesitate to give 2 Gm. for severe spasm and accompanying pain. It should be followed by oral administration and we believe that adequate oral dosage begins with at least 2 Gm. q.i.d., instead of the recommended 1 Gm., q.i.d. Methocarbamol relieves spasm by blocking the multisynaptic reflex pathways (internuncial pool) in the spinal cord.

(c) There are some few promising reports from the use of carisoprodal (Soma) in this condition, but our experience with it has been slight.

(5) *Local block therapy.* When there is a trigger mechanism with trigger zone and reference pain area, it can be relieved by either infiltration with a local anesthetic or by spraying the overlying skin with ethyl chloride. As expressed in reference to the use of methocarbamol, the theory underlying this type of treatment is that the entire symptom complex is an expression of reflex mechanisms which, when once initiated, are self-sustaining by implication of closed self exciting chains of internuncial neurons in the central nervous system. Interruption of the pain cycle with blocking procedures, even though with only transitory action, may abolish the complex permanently. To apply this method successfully it is necessary to have knowledge of the patterns of various syndromes and the location of the trigger areas. Treatment is directed toward the trigger area. Either 0.5 or 1% procaine is used. Occasionally, 0.5 to 1 cc. of prednisolone (Hydeltra) is used after infiltration with the local anesthetic.

The technic of using the ethyl chloride spray is quite simple. The trigger area is located and the bottle of ethyl chloride is held 12 to 18 inches from the skin and the spray applied at an acute angle, the stream being passed over the trigger area in one direction —from the trigger area to the reference zone. The spraying is done with even sweeping motions as in painting a wall. Fifteen or twenty sprayings may be necessary, but usually one or two are sufficient. During the spraying, slight pressure is exerted to produce passive stretching of the painful muscle. It should be remembered that ethyl chloride is inflammable and explosive and adequate precautions are indicated. We do not believe there is any advantage of ethyl chloride spray over injections of procaine.

(6) *Use of (Tubadil) tubocurarine chloride.* In selected cases of intense spasm and pain resultant therefrom, the use of tubocurarine affords considerable relief and probably should be used much more than it is at present. The usual precautions should be observed.

(7) *Ultra-sound.* Norman[17] treated 432 cases of "fibrositis" with ultra-sound and reported an astounding effective result of 96%, but he did not define clearly and exactly what type of cases were included in the "fibrositis" series. Rubin[18] states that ultra-sound is particularly useful in trigger areas which are first injected with lidocaine and hydrocortisone. Covalt[19] finds it difficult to determine which patients will receive relief from ultra-sound; if no benefit is received after six treatments given on alternate days, further benefit is rarely to be expected. Fountain and associates[20] measured the force necessary to initiate movement in spasm of the neck muscle due to fibromyositis and in tightness of the hamstrings in polio patients, and studied the effect of ultra-sound, hot packs and infrared radiation in alleviating such spasm. It was found in the polio patients that hot packs were significantly the most effective and ultra-sound significantly the least effective in the instances of neck muscle spasm. I have not yet seen any carefully documented report of controlled studies using ultra-sound in the treatment of this condition.

(8) *Excision of nodules.* This may be done when indicated (chiefly in the case of herniated fascial fat).

(9) *General management.* Not all patients respond readily to such treatment programs. In many the response is slow, incomplete and only temporary, but there are those in whom these simple measures provide relief of pain and disability in a manner as dramatic as one is likely to encounter in general practice. It is

believed that in quite a few cases psychotherapy is of importance because of the dominant etiologic role played by emotional tension. Since so-called chronic trauma, secondary to poor posture, is also a factor, a program of exercises to strengthen the involved muscles should be instituted when indicated. It is believed that patients with this syndrome should be protected against an undue amount of chilling, dampness and sudden changes in temperatures.

Summary

The present-day classification and terminology used for "fibrositis" is most confusing and inconsistent. The term "myofascitis" (myofascial pain syndrome), seems more appropriate than so-called "intramuscular fibrositis." It is not thought that such conditions as bursitis, tendinitis, periarthritis, neuritis or panniculitis belong in this classification.

The true nature of the cause and lesion of myofascitis remains mostly obscure. The treatment is basically symptomatic and is largely accomplished through physical medical modalities.

Myofascitis or the various myofascial pain syndromes, however, are to be recognized as definite clinical entities and should be appreciated as such. The recognition is not difficult, especially by those who seek for the signs when the symptoms are suggestive. The disease is not uncommon and should be looked for in all cases of pain involving the musculoskeletal system.

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The Diagnosis and Medical Management of Pancreatitis and Its Complications

THOMAS D. DAVIS, JR., M.D., JAMES W. McBEE, M.D., WILLIAM W. SHINGLETON, M.D., and JULIAN M. RUFFIN, M.D.,†
Durham, N. C.

Diagnosis and management of both acute and chronic, or relapsing pancreatitis continue to remain a problem for the family doctor. This concise consideration of these aspects should be filed for quick reference.

Introduction

THE SUCCESSFUL MANAGEMENT of any disease is dependent, to a large extent, upon correct diagnosis. This is especially true of pancreatitis, which of all the diseases of the gastrointestinal tract is often the most difficult to diagnose. The acute attack may be confused with coronary occlusion, perforated ulcer, biliary colic or many other intra-abdominal emergencies. When jaundice is present an erroneous diagnosis of carcinoma of the pancreas or common duct stone may be made. Recurrent attacks of pain, so characteristic of chronic relapsing pancreatitis, may be misinterpreted in the obviously neurotic patient, especially when all studies are negative. It is often assumed that such cases are psychiatric problems, and exploratory laparotomy is not considered. The malabsorption syndrome usually is associated with diffuse disease of the small intestine, but pancreatic insufficiency may produce an identical picture. It becomes a matter of practical importance, therefore, that the physician be familiar with pancreatitis in all of its manifestations so a correct diagnosis may be made and proper treatment instituted.

The Acute Attack Diagnosis

History. As with most diagnostic problems in gastroenterology, one relies heavily upon the history. Although asymptomatic attacks do occur, the clinical picture frequently is so characteristic as to be diagnostic. The predominant feature of the attack is pain. This is located in the mid- or upper abdomen with radiation around the rib cage or straight through to the back and above the level of the iliac crests. It is usually deep and boring in nature with all degrees of severity, aggravated by food, lasting for hours or days and requiring narcotics for relief. Nausea and vomiting are common and residual soreness is the rule. The patient may bend over a chair or table or lie with knees drawn up and arms wrapped around them, the so-called "pancreatic posture." The history of an attack described above, if reliable, justifies the presumptive diagnosis of pancreatitis.

Physical Examination. The characteristic posture, when present, is an important physical finding. Upper abdominal tenderness with muscle guarding is apt to occur and may be accompanied by shock. Varying degrees of jaundice may be present, and occasionally a mass is palpable in the upper abdomen. It should be emphasized, however, that the physical examination may be entirely negative.

Laboratory Findings. A significantly elevated serum amylase is diagnostic, but what constitutes a significant elevation is a matter of individual interpretation. Five hundred Somogyi units or more should be accepted as evidence of pancreatitis and less than 200 of questionable significance. Levels lying midway between may be difficult to evaluate. Obviously, different standards will exist in

†From the Departments of Medicine and Surgery, Duke University Medical Center, Durham, N. C.

different laboratories, and no arbitrary figure can be used as applicable to all cases. Urinary amylase is likewise of value and may remain elevated for several days following an acute attack. Determinations of serum lipase and trypsin have been advocated by some authors but are not generally employed. A significant fall in serum calcium occasionally occurs, and hyperlipemia may be seen.

A well-known, but little used procedure in the diagnosis of pancreatitis is abdominal paracentesis. This may be done easily in the home or office, using local anesthesia and a long, small gauge needle. Demonstrable ascites is unnecessary, as only a small amount of fluid (0.5 to 1.0 cc.) will suffice for analysis. The amylase levels of peritoneal fluid may be markedly elevated (500 to 1,000 units) at the same time that the blood amylase is normal and persist as long as 3 to 5 days after an acute attack. A high amylase content of free peritoneal fluid, when present, is diagnostic of pancreatitis provided perforation or infarction of the stomach or intestines can be excluded.

X-rays. Calcification of the pancreas, when present, is diagnostic of long standing disease. When acute pancreatitis is suspected, a small amount of fluid in the left chest is a helpful finding. Widening of the duodenal arc or the "reversed 3" sign may be present and anterior displacement of the stomach points to a mass in this region. Visualization of the gall bladder by intravenous cholangiography is helpful in distinguishing between cholecystitis and acute pancreatitis.

Management

It is now generally agreed that the acute attack is best treated medically with the following objectives in mind: (1) relief of pain; (2) treatment of shock; (3) correction of electrolyte imbalance; and (4) resolution of the underlying process.

(1) *Relief of Pain.* Although the attack may be mild and require little or no treatment, pain usually is severe, and its relief mandatory. Nothing takes the place of narcotics, the time-honored drug being morphine or its derivatives. It is now well known that morphine may produce spasm of the duodenum, the biliary and pancreatic ducts and the sphincter of Oddi; and on theoretical grounds, its use may be questioned. Therefore, meperidine (Demerol), which is much less likely to cause smooth muscle spasm, is the drug of choice. Other methods of relief of pain have been advocated, such as, (1) procaine hydrochloride given intravenously, (2) paravertebral block, or (3) epidural block. Procaine intravenously is somewhat hazardous and nerve blocks have not been uniformly successful. Nitrites have been used with variable results.

(2) *Treatment of Shock.* Fortunately, shock is uncommon, occurring chiefly in the acute hemorrhagic form. The usual methods of combating shock are employed. Intravenous saline or glucose, transfusions, serum albumin or other plasma expanders, and pressor agents, in addition to elevation of the foot of the bed all may be indicated.

(3) *Correction of Electrolyte Imbalance.* Fluid and electrolyte disturbances are rarely a problem. These disturbances result chiefly from vomiting or gastric aspiration with inadequate replacement. The principle ion concerned is potassium and, therefore, the development of hypokalemia should be kept in mind and prevented by appropriate measures. Hypocalcemia with tetany may be present and requires treatment with calcium intravenously.

(4) *Resolution of the Underlying Process.* The importance of this aspect of therapy cannot be over-emphasized, not only in the supportive treatment described above but in prevention of further destruction of the gland. Anything which puts the pancreas at rest and suppresses stimulation of its exocrine function is desirable. Since the presence of acid gastric juice in the duodenum is a powerful stimulus to secretion, constant gastric suction is indicated. Suppression of vagal stimulation by the use of anticholinergic drugs or other blocking agents is likewise advisable. Carbonic anhydrase inhibitors suppress bicarbonate secretion by direct action upon the acinar cells and are of theoretical value. Although pancreatitis is not primarily an infectious process, there may be secondary invading organisms and, therefore, antibiotics or sulfonamides usually are advocated. Steroids have been advocated by some, but their role in the treatment of pancreatitis has yet to be established. The duration of treatment described above will depend entirely upon the

clinical response, but in most cases can be discontinued after 24 to 72 hours.

Hypothermia has been reported as life-saving in experimentally induced pancreatitis in dogs as well as in several patients having a severe form of the disease. This is still experimental, however, and final evaluation of this form of therapy must await a wider experience than is now available.

The role of surgery following clinical recovery is fairly well established. If the patient is known to have gallstones, operation is indicated with the purpose of removing the gallbladder and exploring the common duct. The demonstration of a mass by palpation or the displacement of the stomach anteriorly by x-ray may justify operation, as such patients probably have a pseudo-cyst. Otherwise, laparotomy is hardly indicated after a single attack.

Recurrent Attacks

The diagnosis and management of the recurrent attack is the same as that of the initial episode, with the single exception,—beware of narcotic addiction! After repeated attacks the problem again arises,—when should the patient be explored? It is reasonable to advise exploration in all patients having chronic relapsing pancreatitis in the hope of carrying out some definitive procedure. The type of surgery to be performed would be determined by the findings on exploration and is beyond the scope of this discussion.

Interim Phase

Since dietary indiscretions and over-indulgence in alcohol are generally accepted as important factors in precipitating recurrent attacks, moderation in eating and drinking is mandatory. In fact, some authors believe that alcohol is to be strictly forbidden. There is little to suggest that pancreatitis is a psychosomatic disease, yet the role of emotional crises in precipitating a recurrence is to be borne in mind. Actually, during the interim phase, one may lead a reasonably normal life.

Pancreatic Insufficiency

While pancreatic insufficiency may be a transitory phenomenon during an acute attack, due either to suppression of glandular function or to ductal obstruction, its development usually indicates extensive destruction of the gland.

Diagnosis.

History. The most constant feature of pancreatic insufficiency is weight loss, which occurs in spite of a normal or excessive food intake. The patient may or may not have diarrhea; gross steatorrhea occurs only in the advanced stage. Malabsorption associated with a history suggesting chronic relapsing pancreatitis points to pancreatic insufficiency as the most likely cause, and the presence of diabetes makes this diagnosis more certain.

Physical Examination. There are no physical findings characteristic of exocrine pancreatic insufficiency *per se*. Complications of diabetes, such as peripheral neuropathy or diabetic retinopathy are rare, but when present in patients having steatorrhea would suggest pancreatic insufficiency.

Laboratory Findings. Although diabetes may be absent, a diabetic glucose tolerance curve in patients suspected of having pancreatic insufficiency is an important finding. The diagnosis, however, is dependent upon the demonstration of impaired digestion of carbohydrates, proteins, or fats.

(1) *Carbohydrates.* The starch tolerance test has been advocated by some, although the results are often misleading and the test has not been generally accepted. The secretin test, when positive, is acceptable evidence of pancreatic insufficiency, but this is difficult to perform and hardly practical in the average laboratory.

(2) *Proteins.* Meat fibers in the stool are indicative of impairment of trypsin activity, but can occur in such conditions as gastrocolic fistula or extensive resection of the small bowel. I^{131}-labeled albumin has been used to demonstrate insufficiency of proteolytic enzymes, but there are certain inherent falacies in the method.

(3) *Fats.* Patients having pancreatic insufficiency invariably have increased fat in the stool. Impaired digestion and/or absorption of fats may be demonstrated by microscopic examination of the feces, fat balance studies, serum carotene, vitamin A tolerance, chylomicron counts and I^{131}-labeled lipid tests. It should be pointed out that excessive fat in the stool may result from disease of the small bowel as well as from pancreatic insufficiency, and therefore it is important to distinguish between the two. The use of I^{131}-

labeled triolein followed by I^{131}-labeled oleic acid has been found most helpful in answering this problem. When absorption is impaired, both blood curves will be flat, with elevated radioactive content of the stools. If the error is one of digestion, only the triolein curve will be flat, with a corresponding elevation of fecal fat, whereas the blood and fecal values of oleic acid will be relatively normal. Thus, marked impairment of triolein absorption with normal values for oleic acid, in the absence of a partial gastric resection, is strong evidence of pancreatic insufficiency.

X-ray Findings. The typical malabsorption syndrome associated with calcification of the pancreas would justify the presumptive diagnosis of pancreatic insufficiency. Since most patients having steatorrhea due to intrinsic disease of the small bowel will have diffuse x-ray changes, a normal ileal study in such cases would again suggest the diagnosis of pancreatic insufficiency.

Management.

Pancreatic insufficiency rarely occurs early in the disease and develops only after repeated attacks with extensive destruction of the gland. This insufficiency may be endocrine, exocrine, or both.

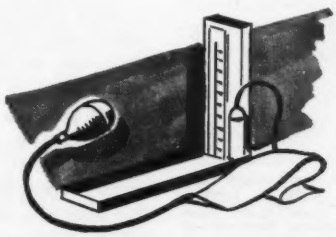
(1) *Endocrine.* Disturbance of carbohydrate metabolism usually antedates the development of frank steatorrhea or even laboratory evidence of exocrine insufficiency. Diabetes in such cases is likely to be mild and easily controlled.

(2) *Exocrine.* Although the pancreas secretes proteolytic and amylolytic as well as lipolytic enzymes, for practical purposes one is concerned primarily with impairment of fat digestion and the development of steatorrhea. This is due not only to the high caloric value of the fat which is lost in the stool, but also to the loss of the fat soluble vitamins and certain minerals. It is wise, therefore, to look for and correct any of these deficiencies which may occur, especially those of vitamin K, iron, or calcium.

The old concept of restricting dietary fat because of the observation that steatorrhea is aggravated by the ingestion of lipids has been replaced by a more intelligent approach to the problem, namely the correction of the digestive deficiency. Various extracts of the pancreas such as Viokase, Entozyme, and more recently, Cotazym have been used. Preliminary observations using Cotazym as replacement therapy have been encouraging. Impaired absorption of I^{131}-labeled triolein may revert to normal when Cotazym is added to the test meal, and prolonged administration of this material has resulted in cessation of the diarrhea and significant weight gain in a small group of patients.

Summary

The diagnosis of pancreatitis should be suspected by history and confirmed in most cases by appropriate studies. Except in the acute hemorrhagic type, proper treatment of the acute attack is gratifying, prompt recovery being the rule. Exploration should be seriously considered in all patients having chronic relapsing pancreatitis, as definitive surgery may bring about improvement or complete recovery. The presence of pancreatic insufficiency can be readily established by the use of I^{131}-labeled lipids, and replacement therapy, using a potent pancreatic extract is highly effective.



The Use of Fat Emulsion Intravenously in the Control of Hemorrhage Due to Thrombolysin Activity*

ALBERT W. BIGGS, M.D., MARION DOUGDALE, M.D., and SAMUEL L. RAINES, M.D.,† *Memphis, Tenn.*, and LOUIS G. NEFT, M.D., *Champaign-Urbana, Ill.*

The authors have considered the mechanism of thrombolytic activity as related to prostatic disease and hemorrhage which may result. They give their experience with the use of fat emulsion intravenously in the control of this form of postoperative hemorrhage.

POST-PROSTATECTOMY HEMORRHAGE has been one of the major problems in urology. Though this has been minimized by improved surgical technics, readily available bank blood, and various forms of drug therapy, there is still the patient who bleeds unexpectedly and in whom the bleeding is not readily controlled by usual measures. We would like to call attention to thrombolysis or fibrinolysis as a cause of hemorrhage under these circumstances and to suggest the use of fat emulsion intravenously and orally as a specific form of therapy.

The urologist has been interested in this problem since 1952, when Tagnon and associates[1] published the first report upon the occurrence of fibrinolysis in association with carcinoma of the prostate. In the 2 cases described, fibrinolysis was demonstrated prior to any attempt at operation. They treated the patients with transfusions and large doses of estrogens. In a later study[2] they found that 6 of 48 patients with carcinoma of the prostate exhibited some degree of fibrinolysis. They also demonstrated that prostatic tissue contained an enzyme capable of digesting fibrin and fibrinogen.[2,3] Ten years before this, Huggins and Vail[4] described fibrinolysis by prostatic fluid.

The problem was again discussed by Lombardo in 1957 and 1958. In his first paper,[5] he recommended the use of fibrinogen for specific therapy. In his second paper,[6] he described 4 cases of carcinoma of the prostate with low fibrinogen levels and fibrinolysin activity. In these cases he thought fibrinogen and a toluidine blue preparation were effective in treatment.

The problem of activation of a fibrinolytic system is not limited to the field of prostatic surgery. It has been described in pulmonary, cardiac, pancreatic and other forms of surgery.

MacFarlane[7] described increased fibrinolytic activity in 70% of patients after operations. In a later paper, MacFarlane and Biggs[8] concluded that mental stress preceding surgery, rather than the operation itself, was the stimulus for increased fibrinolytic activity. There are many known agents which may activate the system, i.e., epinephrine, vitamin K, nicotinic acid, para-aminobenzoic acid, acetylcholine, procaine, phenylbutazone, acute anxiety, strenuous exercise, pyrogenic reactions and many others.

The fibrinolytic system is complicated and there are varying degrees of activity. Marked reaction as demonstrated by lysis of *whole blood* clot is not the common situation. The lesser degrees of activation are more difficult to determine and are probably more common than generally realized. This system, though rather complex, tends to remain in balance because the naturally occurring inhibitors in plasma exceed the potential fibrinolytic activity.[9] There are also a number of known

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†From the Departments of Urology and Hematology, University of Tennessee College of Medicine, Memphis, Tenn.

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Intravenous fat emulsion (Lipomul) used in this study was supplied by The Upjohn Company, Kalamazoo, Mich.

synthetic inhibitors of the system. Interest has been developed recently in epsilon-amino caproic acid which has proven to be a powerful inhibitor of fibrinolysin and also inhibits activation of profibrinolysin.[10]

The role of fat in the system is not clear at this time. The idea of using intravenous fat emulsion was derived from an article by Cliffton[11] in which he stated, "We, ourselves, have shown that a high fat meal will inhibit the excessive fibrinolysis occurring in a case of carcinoma of the prostate with hemorrhage. The same is true of fat infusions." Kwaan, Lo, and McFadzean[12] demonstrated inhibition of fibrinolysis by cholesterol in clots produced experimentally in marginal veins of the rabbit's ears. Greig[13] felt that a fatty meal, especially one high in saturated fats, would inhibit fibrinolysis.

Bang,[14] in unpublished data, has some experiments and electron photomicrographs which lend evidence to the view that the action of fat is not that of an inhibitor but a protector. Clots made in a lipemic environment are structually different from normal clots. These clots appear to be very resistant to the activity of fibrinolysin as compared to a control normal thrombus. A recent personal communication from Dr. Sol Sherry,[15] relates " . . . though lipids have been claimed to be inhibitors of the fibrinolytic system, the evidence along this line is still some what inconclusive. . . . observations, though not definitive, suggest that perhaps lipids do not inhibit the fibrinolytic enzyme system, but that clots formed in the presence of lipids may be much more resistant to subsequent enzymatic lysis."

We have used fat emulsion intravenously supplemented with fat orally in 5 patients with prostatic disease who showed marked fibrinolysis activity. Four of these patients had carcinoma of the prostate and one had a benign prostatic hyperplasia. Fibrinolytic activity was suspected when unexpected hemorrhage developed. A tube of clotted blood was observed for lysis of the clot over a period of 4 to 8 hours. If lysis was demonstrated by this method, incubated clots were observed and routine clotting studies were performed.

Intravenous fat emulsion was given and serial clots were incubated at 37° C. and observed. A high fat diet was given when tolerated.

Case Reports

Case 1. S. H., a 55 year old colored man, was admitted to the John Gaston Hospital because of acute retention. Examination revealed generalized carcinomatosis. Rectal examination was characteristic of prostatic carcinoma with local extension. Matted nodes were palpable in the inguinal, femoral, axillary and cervical areas. X-ray views of the chest and abdomen revealed extensive osteoblastic metastases. A cervical node biopsy was reported as showing adenocarcinoma, probably prostatic in origin.

Transurethral resection of the prostate was done to relieve the obstruction. Four hours after operation, the patient began to bleed profusely from his urinary tract and from old wounds of antecubital vein puncture. The usual methods to control the bleeding were tried. These included tension on the catheter, frequent irrigations, transfusions, fibrinogen, hormones, steroids and vitamins. Hematologic consultation was obtained. The clotting mechanism was normal but there was 30% clot lysis in 2 hours. The consultant suggested the use of fat emulsion intravenously on the basis of Cliffton's experience in one case.[11] Two units (1,000 cc.) of intravenous fat emulsion were given with no untoward reaction. Within 6 hours, the hemorrhage had ceased and clot lysis *in vitro* was no longer demonstrable.

Case 2. J. B., a 78 year old colored man, was admitted to John Gaston Hospital because of acute retention. Examination revealed an uremic patient with inoperable prostatic carcinoma. He was placed on catheter drainage and given general supportive therapy. Seven days later he developed a severe hemorrhage from the urinary tract. The clotting tests were essentially normal. Clot lysis was 50% in 4 hours. One unit (500 cc.) of intravenous fat was given with control of hemorrhage and fibrinolysis in 6 hours.

Case 3. J. W., a 67 year old Negro with known carcinoma of the prostate for 7 years, was admitted in urinary retention. He had previously had a transurethral resection of the prostate and orchiectomy. For 7 years he had taken 5 mg. of diethyl stilbesterol daily.

Preoperative study revealed some increase in fibrinolytic activity. The patient was placed on a high fat diet for 4 days prior to operation. Immediately following a transurethral resection, clot lysis was noted to be 30% in 3 hours. At this time a profuse hemorrhage started in the prostatic fossa, meatotomy and venipuncture wounds. One unit of fat emulsion was given and the bleeding was controlled. On the next day, a second hemorrhage started and again fibrinolysis was demonstrated. This also responded to the administration of fat emulsion. The patient has been kept on a high fat diet since with satisfactory control of fibrinolytic activity.

Case 4. V. J., a 71 year old colored man, was admitted with a 12 month history of chronic urinary tract obstruction. Examination revealed carcinoma of the prostate with extensive osteoblastic metastasis. The prostate was resected in two stages. The first was uneventful. The second stage was complicated by fibrinolysis manifesting itself in both cerebral and prostatic hemorrhages. *In vitro* lysis was demon-

strated. Three units (1,500 cc.) of fat emulsion were given with cessation of fibrinolysis in 13 hours.

Case 5. L. S., a 59 year old Negro, was admitted because of chronic urinary tract obstruction and acute retention. No evidence of prostatic carcinoma was noted. Examination of prostatic tissue removed later confirmed the diagnosis of benign prostatic hyperplasia. Several hours after the resection of the prostate, profuse prostatic hemorrhage and hemoptysis developed. Steroids, hormones and vitamins were given to no avail; 30% clot lysis was noted in 2 hours. One unit (500 cc.) of intravenous fat emulsion was given with control of bleeding and fibrinolysis in 5 hours.

Discussion and Summary

Activation of the fibrinolytic system may be a serious complication in the patient with prostatic disease. It may occur in the preoperative as well as in the postoperative state. It is not limited to patients with prostatic carcinoma but may occasionally occur in men with benign prostatic hyperplasia. The mechanism by which this occurs is not known. There may be several factors which alone or in combination can trigger the reaction. Acute anxiety, preoperative medication, anesthesia, release of prostatic tissue kinases, bacteremia, anoxia, hypervolemia, and absorption of urokinase could be the activator.

Hemorrhage due to fibrinolysis does not respond readily to the usual hemostatic measures. Intravenous fat emulsion has controlled both the hemorrhage and clot lysis in the five cases reported. Though the mechanism is not clear at this time, there is enough presumptive evidence to suggest that clots formed in the hyperlipemic plasma may be resistant to proteolytic activity.

In our experience, intravenous fat emulsion, supplemented when possible by oral fat, has been an effective and inexpensive agent in the control of hemorrhage when due to fibrinolysis.

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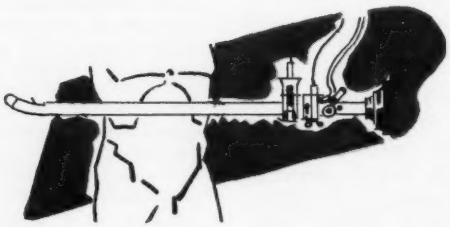


Dislocation of the Radial Head with Associated Fracture of the Ulna

(Monteggia Fracture)*

VIRGIL R. MAY, JR., M.D., and WILLIAM MAUCK, M.D.,† *Richmond, Va.*

The authors point to this type of lesion as occurring in about 10% of instances of fractures of both bones of the forearm. The need for open reduction for an adequate functional result is stressed.

THE BENEFITS AND ADVANTAGES of the use of the intramedullary nail and well-fitting plaster casts are apparent with this fracture dislocation. There are two major entities to consider in recommending and formulating planned therapy in the Monteggia fracture. Not only must one consider the dislocation of the radial head from the capitellum of the humerus, but one must take into account the fracture of the ulna.

This fracture dislocation was first introduced into medical literature by Giovanni Batista Monteggia, an Italian, who told of it in his last works in 1814. More than one case had been seen by him in which there was dislocation of the radius associated with fracture of the ulna.[1,2]

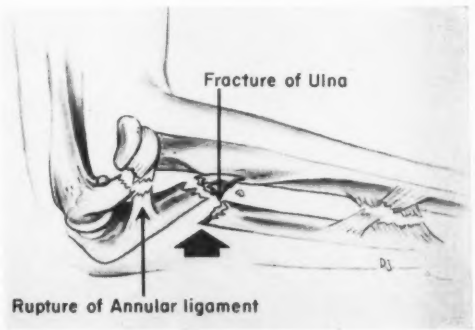
This paper discusses the injury and emphasizes the importance of accurate diagnosis and prompt treatment. It occurred to us how easily this entity might go unrecognized in its fullest extent, when recently 2 patients were admitted to the Medical College of Virginia, and not long before a patient had been seen 3 weeks following a "closed reduction" with the resultant fracture-dislocation still present. These cases stimulated our interest in the investigation and study.

Incidence and Etiology

The injury is not uncommon and makes the physician cognizant of the importance of an accurate early diagnosis. The fractured ulna is easily recorded but the complete dislocation of the radial head either anteriorly or laterally may be misjudged. Failure in the latter instance can result in permanent disability in function and in permanent deformity to the elbow.

Usually the force which causes the ulna to fracture with dislocation of the radial head is by direct posterior violence to the forearm, such as, falling on one's forearm, throwing the arm up to protect one's head, or being involved in an automobile accident. It has been our experience that there is a rather high incidence of compounding of the ulna due to its subcutaneous location (Fig. 1). To sustain such an injury the mechanism of force is great, as compared to other fractures of the forearm. The ulna is generally fractured in its more substantial portion, namely, the upper third. In the child it is frequently of a greenstick type but in the adult it is usually transverse and comminuted.

FIG. 1



Drawing illustrates the mechanism of force to cause the injury. The annular ligament and interosseous membrane are torn. The radial head is dislocated.

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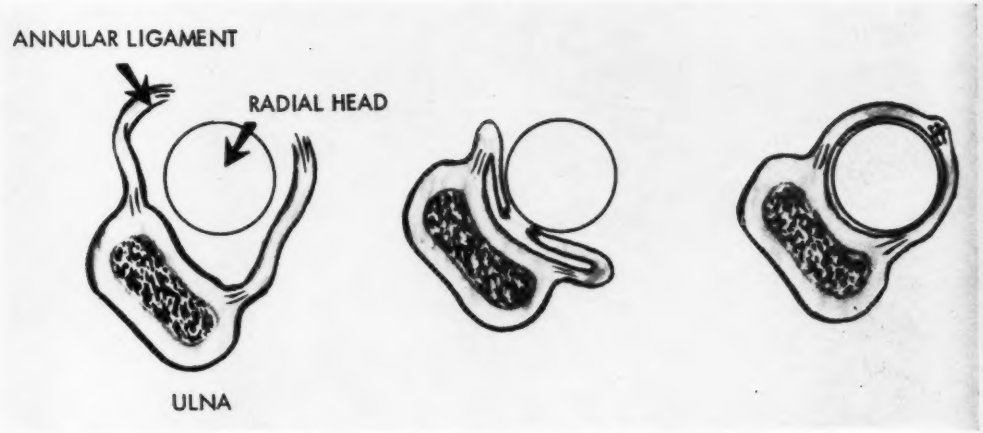
†From the Department of Orthopaedic Surgery, Medical College of Virginia, Richmond, Va.

FIG. 2



This drawing demonstrates the possible positions of the annular ligament in relation to the radial head.

Pathology

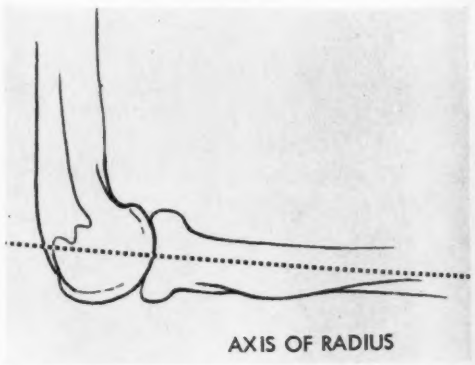
The dislocation of the radial head first ruptures through the annular (obicularis) ligament. This tear varies as to the position of the radial head at reduction, depending upon the amount of the dislocation which may have occurred initially. The x-ray findings will not be of value to the physician as to the position of the annular ligament. Smith[2] showed that the annular ligament may present one of three types of lesion. The ligament may be torn across and remain open (Fig. 2). The ruptured ends may tuck themselves behind the radial head on reduction, or the head may pull itself completely out of the annular ligament. We have observed the first two of these lesions in the annular ligament, but it is not too feasible for the radial head to pull out of the annular ligament, since the ligament fits snugly against the mushroom head of the radius. It is good surgical judgment to investigate the ligament if there is the least doubt as to whether or not, on reduction of the ulna, the radial head is reduced and remains reduced on carrying the elbow through its range of motion (Fig. 3).

In addition to the lesion of the annular ligament, the interosseous membrane between the radius and ulna is expected to be torn. The pull of this membrane and the direction of force angulates the ulnar fragments anteriorly. The muscle pull of the supinator and the anconeus tend to continue deforming the ulna angulation in spite of attempts at closed reduction and application of a cast. Smith and Sage[3] in their work have shown that even with intramedullary fixation there may be angulation at the fracture sites of the bones of the forearm. With adequate reduction of the radial head this is minimal.

Diagnosis

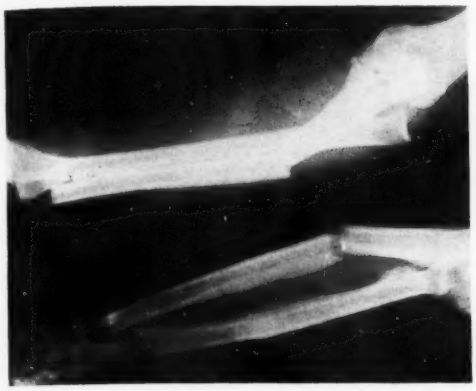
In making the diagnosis which is impossible by examination alone, the physician has to have good x-ray studies. These films must include the elbow as well as the wrist. Many associated fractures of the distal forearm are present with the fractured ulna and dislocated radial head (Figs. 4 and 5). Failure to use the x-ray may lead to a rather grave error in judgment. Careful physical examina-

FIG. 3



The diagram demonstrates the position of the radial head to the capitellum of the humerus. The axis of the radius always passes through the capitellum of the humerus.

FIG. 4



Anteroposterior and lateral views showing the importance of including the entire forearm on the film. In addition to the fracture dislocation near the elbow, there is a fracture of the distal radius and ulna.

tion will usually reveal the true picture to the clinician. The radial head is practically always palpable anterior or lateralward to the lower end of the humerus if it is either dislocated or subluxated. Rotation of the forearm, both in supination and pronation, is limited and very painful at the elbow.[4]

Whenever there is a fracture of the ulna with even minimal angulation, one should suspect a subluxation or dislocation of the radius. It has been said by others, whenever a child has a greenstick fracture of the upper one third of the ulna one should obtain comparison studies of the opposite elbow to determine the exact location of the radial head.

Treatment

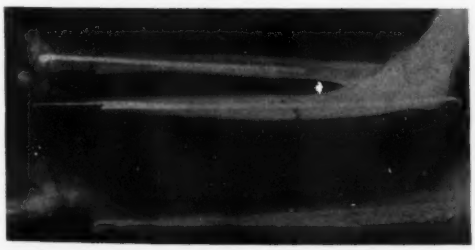
It is our opinion that most all of the patients presenting themselves with a dislocated radial head and fractured ulna should have an open reduction and to be followed by a long arm cast with the elbow in flexion and the forearm in some supination. There may be some of these which can be reduced by closed means and maintained satisfactorily, but they are rare even in children when there is only a greenstick fracture of the ulna with some angulation, and the radial head only subluxated. In these the maintenance of position is difficult. Therefore it will be necessary to make frequent x-ray examinations after reduction. If there is either more angulation at the fracture site or the head of the radius becomes displaced, open reduction is mandatory. We recommend that open reduction be done when this fracture dislocation is observed.

In performing an open reduction we have used the intramedullary rod in the ulna, and frequently have repaired the annular ligament following reduction of the radial head dislocation. The ulna must be anatomically reduced and maintained.

Not infrequently we have employed the use of a Kirschner wire introduced posteriorly through the capitellum of the humerus into the head of the radius to assure maintenance of reduction. This is withdrawn in 4 weeks, at which time a new close fitting cast is applied to the arm. A cast, as a rule, is worn for 6 weeks following the reduction, depending upon the x-ray findings as to the healing of the ulna. Should the fractured ulna be compounded, open reduction is done immediately.

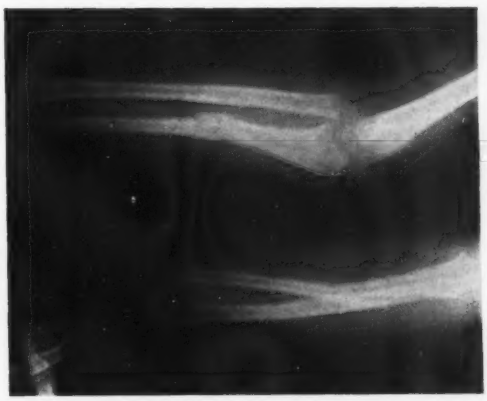
An incision over the lateral inferior head

FIG. 5



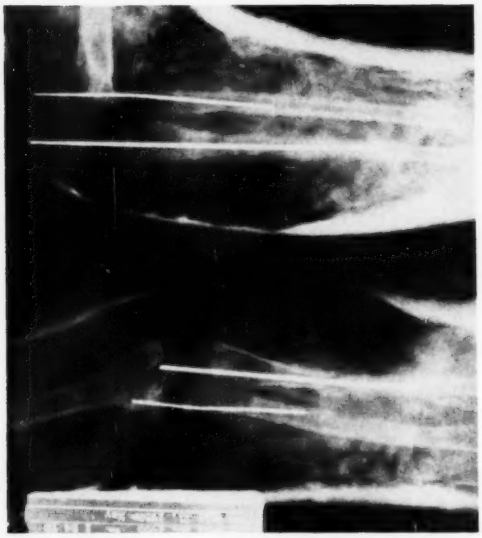
Postoperative films reveal the reduction of the fractures and the dislocation.

FIG. 6



Anteroposterior and lateral views of a 3 year old child treated by closed reduction 3 weeks prior to open operation. Note angulation of ulna with callus formation and the associated dislocation of the radial head.

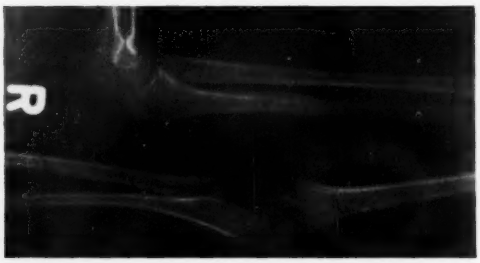
FIG. 7



Postoperative films show the reduction with Kirschner wire through the radiohumeral articulation.

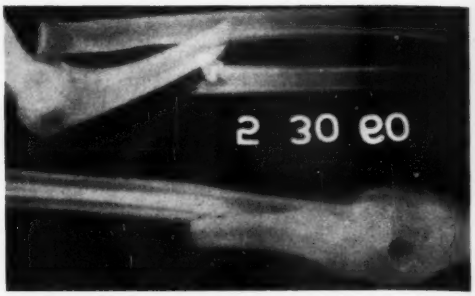
of the radius is made so the annular ligament can be investigated and repaired. On occasion it has been necessary to use heavy catgut suture to simulate the annular ligament. A fascial strip may be used from the operative site. This has been described by Speed and Boyd,[5] though we have not found this necessary in our cases (Figs. 6-8). No bone plates have been used nor are they advocated since the intramedullary rod has proved excellent. Insertion of the pin is easier and associated with less operative trauma, and its removal is a minor procedure. Furthermore, the pin permits compression contact of the bone ends.[6] Bone chips are also frequently used about the ulna fracture (Figs. 9-11).

FIG. 8



Three years postoperatively the reduction is maintained. Note the periosteal elevation about the entire ulna.

FIG. 9



Anteroposterior x-rays reveal a typical deformity of the fractured ulna and dislocated radius.

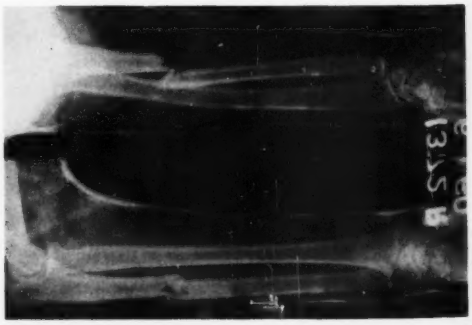
Operative Treatment

The procedure is done with a tourniquet in place. The technic is the same for children as for adults. The recommendation for open treatment is contrary to the statement by Böehler in that all Monteggia fractures can be treated by conservative methods. We would consider this only in rare selected instances.

An incision is made over the lateral humeral epicondyle posterior and passes distally along the posterolateral aspect of the ulna as far as necessary to expose the radiohumeral articulation. The anconeus muscle is reflected subperiosteally from the upper two inches of the ulna. This is done along with the supinator muscle. Reflection of this muscular flap laterally exposes the head of the radius as well as the capitellum of the humerus. The deep branch of the radial nerve is protected in the muscle substance of the supinator[7] (Fig. 12).

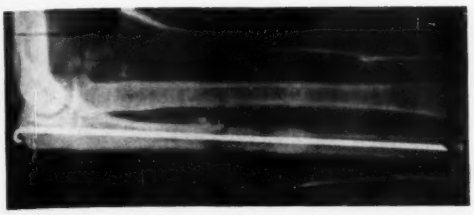
If the fracture of the ulna seems too far

FIG. 10



Anteroposterior and lateral views following closed reduction. The lateral film shows the ulna to be in good alignment. The anteroposterior view reveals the ulna to be unstable due to comminuted fragments.

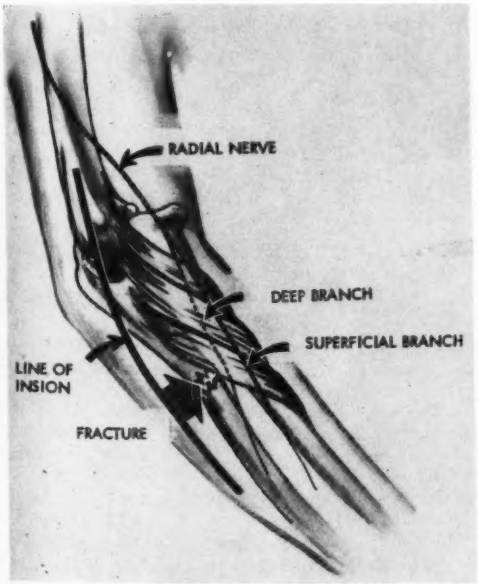
FIG. 11



Lateral view shows the comminuted fragments made into small chips for grafting and the position of the ulna to be stable.

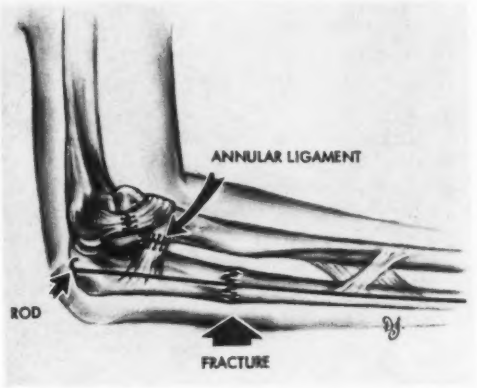
distal, another small incision is made over the fracture site at the subcutaneous area. First we reduce the ulna by means of an intramedullary nail running retrograde. This is anchored at the olecranon. The radius as a rule will reduce itself. The annular ligament is observed, reduced and sutured; or, if destroyed to a great extent is substituted for the ligament by a chromic ligature around the radius and anchored in the ulna (Fig. 13). In some of our cases, to maintain added support in the reduction, a Kirschner wire was passed through the capitellum into the head of the radius. If this is done the wire is cut one-half inch from the skin edge. Following closure of the wound, the protruding Kirschner wire is padded and not incorporated in the long arm cast. The cast is applied with the forearm at a right angle in some degree of supination. The pin is left in the radius for approximately 4 weeks; a long arm cast is worn for 6 weeks. The patient is then begun on exercises for movement in all directions. Usually there may be some lack of full supination and pronation. This was observed only in the adults.

FIG. 12



The incision is made posterior lateral to the deep branch of the radial nerve.

FIG. 13



Drawing illustrates the annular ligament repaired and an intramedullary rod in the ulna to maintain the reduction of the fracture.

Discussion

Over the past 10 years 17 patients have been seen with dislocated radial heads and fractures of the ulna during which time 142 fractures of both bones of the forearm have been treated in the hospital. The Monteggia fracture represents approximately 10% of the admissions for fractures of both bones of the forearm, and thus is not an uncommon fracture (Table 1).

Nine of the patients were males and 8 were females. Five instances were in children from 3 to 10 years of age. The children obtained their injuries by playgound mishaps, as, falling from sliding boards, skating, bicycling and falling against curbings. The oldest patient was 77 years old, who received his injury in a fall from a ladder.

In our series of patients there were 8 compound wounds of the ulna. In no case did infection develop either in the compound injuries or in the closed cases which were operated upon. All compound injuries had open reductions performed initially except in one;

TABLE 1

SUMMARY OF SEVENTEEN PATIENTS

Case	Sex	Age	Type of Fracture	Length of Time Until Reduction	Associated Injuries
1. G.W.	F	3	Simple	3 weeks	None
2. W.T.	F	6	Simple	1 day	None
3. B.B.	F	7	Compound	4 days	None
4. J.B.	M	7	Compound	Same day	Fracture, lateral epicondyle humerus
5. B.Y.	F	10	Simple	2 days	None
6. C.T.	M	22	Compound	Same day	None
7. J.A.	F	22	Simple	Same day	Fracture, proximal phalanx middle finger
8. W.S.	M	30	Compound	Same day	Radial nerve palsy
9. H.H.	M	30	Simple	Same day	None
10. J.M.	M	32	Compound	10 days	Fracture, ribs
11. C.B.	M	35	Compound	Same day	None
12. M.J.	F	37	Simple	2 weeks	None
13. R.C.	M	43	Compound	Same day	None
14. E.H.	M	49	Simple	Same day	None
15. J.C.	F	55	Simple	Same day	None
16. E.B.	F	62	Simple	Same day	Fracture, radial head
17. S.G.	M	77	Compound	Same day	Fracture, distal radius and ulna

in this case reduction was delayed because of other injuries. In 2 cases open reduction was not done. In one of these removal of the radial head was recommended later when the head redislocated; in this case the elbow was limited in all directions of motion and was painful.

In 11 patients operation was performed on the day of admission, regardless of whether or not the patient had compound wounds. In one case the injury was 3 weeks old before the child was admitted.

There were no other associated injuries in 11 patients. Radial nerve palsy was observed in one patient prior to operation. There were 4 patients in whom transitory palsy was observed following operation, which we believe was due to retraction on the supinator muscle.

Conclusion

1. The Monteggia fracture is not an uncommon one, occurring in about 10% of fractures of both bones of the forearm.

2. If not recognized and properly treated early loss of function and deformity invariably results.

3. X-ray examination must include the full length of the forearm; a view of the lower one third of the humerus and the wrist is mandatory in making the diagnosis.

4. Open reduction of dislocation of the radial head associated with fractured ulna is necessary in adult patients and should be strongly considered in children.

5. A Kirschner wire can be placed through the radiohumeral articulation with impunity to the joint to better secure the reduction of the radius.

6. The incision of Boyd is the safest and best to use for exposure of the radial head and in protecting the branch of the radial nerve.

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Discussion (Abstract)

Dr. Oscar P. Hampton, Jr., St. Louis, Mo. Dr. May has presented well the problems of the Monteggia fracture and I am in general agreement with him. I am most surprised, however, that, even though he comes from the capital of the Cenfederacy, he did not give the synonym "Parry Fracture," as it was called in the War Between the States. Parry fractures were common during that exhaustive conflict because of blows on the forearm with the butt of a gun in the hand-to-hand fighting.

I believe I favor open reduction and internal fixation of these fractures in adults even more than Dr. May. The entire radius and ulna have a fixed functional relationship. The length and design of each must be

maintained. Any actual or relative shortening or angulation of either bone disturbs function of the forearm. Not only will the range of promotion and supination be limited but flexion and extension at the elbow or wrist may be impaired. It is essential, therefore, that full length and perfect alignment of the ulna be restored, and the head of the radius restored to its exact position at the elbow if the best obtainable result is to follow. If the ulna heals in even slight angulation or minimal over-riding, relative shortening of this bone occurs and the function of the humeroradial articulation is impaired even though the radial head may not redislocate.

Usually the fracture of the ulna is somewhat oblique rather than transverse so the indication for internal fixation is self evident. The same quality of internal fixation is needed, however, even though the fracture line is transverse, because an excellent closed reduction with the extremity incorporated in a splendid plaster cast may be lost, as angulation occurs in the cast when swelling has receded and atrophy of the musculature taken place. Internal fixation of the ulna in perfect apposition and alignment is a conservative procedure for Monteggia fractures in adults unless there is some specific contraindication to operative intervention.

Remarks by the Chairman*

T. Paul Haney, M.D., *Tulsa, Okla.*

In September of 1960 there was a most successful Venereal Disease Institute held in Tulsa under the auspices of the U.S. Public Health Service through its communicable disease committee of Atlanta, the Oklahoma State Health Department and the Tulsa City-County Health Department. Participants in this Institute came from Public Health Service, represented by Dr. Evan Thomas, Dr. Gerald Barton, Director of Communicable Disease Services in Dallas Regional Office, and Miss Hilda Nivals, Chief Consultant Nurse in Venereal Diseases, with the Department of Health Education and Welfare, Atlanta, Georgia. Local participants were representatives from the Oklahoma State Department of Health in Oklahoma City, including the State Health Officer, and representatives from the local medical profession, internists and general practitioners, primarily.

From this Institute I learned one thing that I wish to bring to you and that I think is most significant. It is as follows:

From studies made there is indication that venereal disease incidence can be higher among people who have not had the best family influences during their childhood and early adulthood. When family ties break, protection against diseases such as venereal disease and emotional disturbances are decreased. It was brought out in our Institute in Tulsa that the family physician can strengthen family ties and in so doing it is believed that the health of the family will benefit, and this is my point: Private physicians have too often not given time to the family to discuss their problems and help in the solution of same. There is no person in America more capable of helping solve family problems and to strengthen family ties than the private family physician.

I am wondering if there are many family physicians like my old Dad (whom some of you attending this meeting knew in Mississippi) who practiced in the early part of this century. I think there are thousands of physicians today just as good and could be a family physician just as good as he was, if they would take the time from their busy practice to imitate this important type of preventive medicine.

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*Presented before the Section on Public Health, Southern Medical Association, Fifty-Fourth Annual Meeting, St. Louis, Mo., Oct. 31-Nov. 3, 1960.

Carcinoma of the Skin Following Acute and Chronic Trauma*

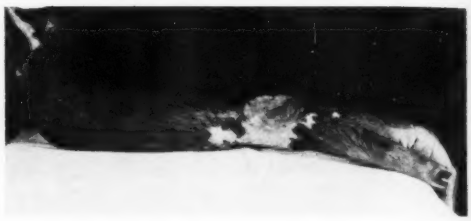
BENJAMIN F. BYRD, JR., M.D., ANTHONY J. MUNOZ, M.D., and HAROLD FERGUSON, B.S.,† *Nashville, Tenn.*

The authors have reviewed what is known about the development of skin cancer at the site of former trauma, as well as the theories which might explain the inherent cellular changes. Their own clinical material is described and evaluated.

OUR INTEREST IN THIS SUBJECT was originally stimulated by the problem of a young negro girl who entered the surgical outpatient department of the Vanderbilt University Hospital with a squamous cell carcinoma arising in a scar from a burn on the forearm. This was an extensive lesion, and at the time amputation was advised (Fig. 1). She refused this but agreed to a local excision of the lesion with a skin graft of the defect. This was unsuccessful to no one's particular surprise. The rather amazing thing was the rapidity of growth of the lesion. She finally submitted to a shoulder girdle disarticulation. This was to no avail and she continued rapidly downhill dying 18 months after the first operation and 12 years after the original injury.

In our study of this patient we went back through the available literature on cicatricial cancer and found that there has been little emphasis placed on the fact that these may be rapidly progressing tumors. Our interest led to a review of all available material at the Vanderbilt University Hospital on cicatricial cancers. From this review it became apparent that there were cancers in which longstanding injury or irritation seemed to play a part. There were also those patients who gave a history of recent trauma followed by carcinoma of the skin. Simply for completeness we reviewed both groups and insofar as possible made a follow-up study of both groups. Among 445 cases of skin cancer diagnosed in the Vanderbilt University Hospital, there were 73 instances of carcinoma directly related by history to some intercurrent injury. Seven of these have been inadequately followed for a variety of reasons and were dropped from the series. The reported group then consists of 66 patients who have been followed to death or the present time.

FIG. 1



These were arbitrarily divided into three groups according to the time elapsed between injury and the diagnosis of the tumor. There were 13 patients in whom this interval was less than 12 months. In 22 patients there was a lapse of from 1 to 10 years intervening between injury and diagnosis. There was a lapse of more than 10 years between injury and diagnosis in the remaining 31 patients. This latter group is made up of so-called "Marjolin" ulcers.

It was of interest to us to find that the term Marjolin ulcer might be more properly changed to verrucous ulcer, or if one still feels compelled to apply a surname to it then Hawkins' or Brodie's ulcer. Marjolin[1] was a contributor to a French dictionary of medical terms. He described these ulcers as follows: "the surface of these ulcers is formed by a tissue consisting of many villous processes, conical in shape, in texture dense and closely packed, resembling somewhat a thick wool

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†From the Department of Surgery, Vanderbilt University School of Medicine, Nashville, Tenn.

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TABLE 1

SOURCE OF ORIGINAL INJURY
(10 Years +)

Vascular	2	(6.5%)
Chronic drainage site	4	(12.9%)
Osteomyelitis	5	(16.1%)
Laceration	5	(16.1%)
Burn	15	(48.4%)
	31	(100%)

velour. From these ulcers oozes in small quantity, a viscous fluid, nearly colorless and fetid, which upon drying forms a thick crust, hard, greyish, and very adherent. The ulcers are not very painful, while at the same time are slow growing and capable of spreading considerably." We suppose that even though Mr. Hawkins[2] first reported instances of this disease and stated that Mr. Brodie (of abcess fame) had removed such an ulcer 7 years before, we must continue to apply the name of Marjolin to whom we are indebted for such a complete description.

Clinical Study

Marjolin ulcers are most frequently found in old scars of burns but actually may occur in any chronic sinus or tract. In the Vanderbilt group the majority of such ulcers were found in old scars of burns. However, 29% occurred in chronically draining sinuses or tracts of one sort or another, usually following osteomyelitis. Of the two injuries which were listed as vascular in origin, one was a stasis ulcer and the other followed a frostbite 7 years before the diagnosis of squamous cell carcinoma was made (Table 1).

The chronic cicatricial group was made up for the most part of squamous cell carcinomas. There were a very few (9.7%) basal cell carcinomas in our cases but somewhat more were mixed in their miscroscopic picture (Table 2).

The patients in this group have been treated in a variety of ways.

Of those who died after treatment, one had a basal cell carcinoma of the face following a laceration. This patient was treated by excision followed by radiation. One patient who died with squamous carcinoma was treated by radiation alone. Another patient had a squamous carcinoma treated by amputation, and the last death due to tumor was an individual who had a mixed basal and squamous carcinoma (Table 3).

TABLE 2

MICROSCOPIC CHARACTER OF CANCER
(10 Years +)

Basal cell carcinoma	3	(9.7%)
Mixed B and S carcinoma	9	(29 + %)
Squamous cell carcinoma	19	(61.2%)

TABLE 3

METHOD OF TREATMENT
(10 Years +)

	Total #	*Died of Tumor*
X-ray alone	1	1
Excision	19	2
Alone	(15)	(1)
+ Radiation	(2)	(1)
+ Node diss.	(2)	
Amputation	9	1

From a review of the method of treatment and survival it may be concluded that these tumors may have a very rapid course. The absolute survival at 5 years is low but this is largely due to deaths from intercurrent conditions. However, these are not relatively benign tumors nor even as slowly progressive as the more frequently encountered epitheliomas (Table 4).

Discussion

The most fascinating aspect of this entire problem is the relation between trauma and cancer of the skin. Ruchaud,[3] in his doctoral thesis in 1905, stated the conditions which he thought necessary for the transformation of a burn scar into cancer. (1) In order for scars to undergo degeneration, it is necessary that the original wound suppurate for a long time or have taken a long time to heal. (2) That the cancerous degeneration of a cutaneous cicatrix cannot take place until 20 to 30 years after the burn; it is not the age of the subject but the age of the scar which intervenes in this phenomenon. (3) After this long delay, if the scar has been left alone, there will not be tumorous proliferation, but if trauma occurs, no matter how insignificant, the tissue equilibrium will be altered and the tumor will appear.

TABLE 4

ABSOLUTE SURVIVAL FROM DIAGNOSIS
(10 Years +)

	No.	*Average Survival*
Dead of tumor	4	1.2 Years
Dead other causes	10	6.8 Years
Living	15	11.5 Years
Absolute Five Year Survival 62.0%		

Experimental as well as clinical observations in subsequent years have shown that there may be some merit in these postulates of Ruchaud.

In 1941, Mackenzie and Rous[4] found that applying carcinogenic tar to the skin of rabbits would render many more epithelial cells neoplastic than manifest themselves by developing into tumors. They found that these neoplastic cells remained dormant in the epithelium until some type of stimulation from a "co-carcinogen" elicited a response which would set the dormant cells into a growth pattern that would produce true tumors. Since that time numerous investigators have shown that treatment of the skin with a carcinogen followed by stimulation with a co-carcinogen may result in tumor production. In this fashion Pullinger[5] and Simpson[6] have used simple acute trauma as the "co-carcinogen." Saffiotti and Shubik[7] studied the production of tumors following burns in mice. They burned areas of the skin in mice, and in a portion of these applied croton oil to the burn area at a later date. Forty-seven per cent of the animals treated with croton oil developed tumors after an average time lapse of 32 weeks. In the animals burned but not treated with oil there was a 7% incidence of tumors, and this after a 63 week interval.

Berenblum[8] studied this same problem by the application of tar as the basic carcinogen followed by croton oil as "co-carcinogen." He obtained a response similar to that of Saffiotti and Shubik.[7] When the same materials in the same quantity were applied in reverse order, the croton oil first and then the tar, no tumors could be produced. He concluded that, "the inception and the completion of the carcinogenic action involved independent mechanisms."

From these facts it seems that one may accept as a working theory the hypothesis of Friedewald and Rous,[9] that there may be a two stage mechanism in the carcinogenesis of skin tumors. The first is the "initiating phase" which is responsible for the conversion of normal cells into dormant cells, and the second the "promoting phase" which is responsible for the encouragement of these dormant cells to develop into tumors. Berenblum[8] has theorized that the normal epithelium there is a dynamic equilibrium of growth, "stem cells" dividing into 50% mature cells and 50% "stem cells." Even in hyperplasia there is an equilibrium of growth but an increased rate of division. In the neoplastic state this equilibrium is upset and more than 50% of the daughter cells remain as stem cells. He concludes from this that the promoting action involves a delay of maturation at the stem cell stage and not necessarily an increase in rate of cell division.

Gillman and associates[10] support a theory advanced by Wolbach[11] in 1909. They believe that conditions in the underlying dermis may result in the development of epithelial neoplasms. They found experimentally that epithelial hyperplasia and invasion of the dermis was controlled by the dermal connective tissue. Disturbances in the connective tissue could result in dermal invasion of the overlying epithelium and in epithelial hyperplasia. They also state that such dermal changes as experimentally cause increased epithelial activity may be seen in both acute and chronic skin injuries, in chronic irradiation injuries, in burning, and in aging skin.

Thus there are postulated two mechanisms by which traumatic cancer may conceivably occur:

(1) A two stage process—the "promoting phase" setting the stage by transforming normal epithelial cells into so-called "dormant cells," and the "initiating phase" causing an activation of these dormant cells into frank neoplasms. (2) Changes in the dermal connective tissue caused by injury which may lead to epithelial hyperplasia and invasion.

If we may first consider "acute traumatic skin cancer," one may postulate that either or a combination of these two processes may be involved in the development of a carcinoma. Clinically, it is known that cancers associated with acute trauma and short latent periods occur more frequently in older age groups. It may be that over the years some factor has had a "promoting" action on the skin and that there are many dormant or latent cells which await activation of an initiating agent. This "initiating" agent may be the trauma which has been, on some occasions, considered to be the "complete carcinogen" and thus the sole cause of the subsequent malignancy.

One may speculate that over the years the aging process of the skin has resulted in changes in the dermal connective tissue which become more severely deranged during the

episode of trauma. The result of this derangement is epithelial hyperplasia and subsequent neoplasia and invasion. Should it be that both mechanisms are involved then it seems logical that a combination of the two may be the process through which skin cancer follows acute trauma in many cases.

Similarly, in the instance of the epitheliomas following the more chronic injuries either or both of the cited processes may obtain. The initial injury may furnish the initiating action. The promoting agent may be one or a combination of many agents to which the original site of the injury is exposed over the long latent period. This promoting action may be due to any irritant—subsequent trauma, sunlight, dye stuffs, or various chemicals. On the basis of our other hypothesis the initial injury may alter the dermal connective tissue to such a degree that further insults to the integrity of the tissue (aging, trauma, etc.) may cause sufficient derangement to lead to carcinogenesis. It does seem to us that the classic two stage process of carcinogenesis which takes place in the Marjolin or chronic cicatricial type of epithelioma may offer some clue to the occasional skin cancer which is seen following an acute trauma. The third postulate of Ruchaud may express the true course of events which relates the initiating and promoting phases of skin carcinogenesis.

There is in reality no evidence at any point in the whole mass of experimental data to support a belief that a single injury can result in the development of a skin cancer.

The distribution of the lesions that were involved in the total group of cancers in the Vanderbilt series that were related to trauma is seen in table 5. The distribution by body areas follows relatively closely the distribution that has been found by various other authors in series of cancers related to trauma.[12-16] The striking difference in comparing the traumatic group to nonselective series is the relatively greater proportion of those tumors which are related to trauma that occur in areas other than the face.[17-19] The portion of the series reported by Schrek[20] most nearly follows our own group when those tumors related to scars are considered.

Our Group I and II tumors seem to arise predominantly in the areas which seem not predisposed to nontraumatic cancer. These facts may be interpreted to mean that the usual sites of skin cancer have a ready and waiting malignant potential and thus a short latent period is required for the development of the cancer. The rarer sites need more stimulus and thus have a longer latent period for the malignant change to become established.

The distribution of the Vanderbilt University Hospital series by sex is not remarkable. There were 48 males and 18 females. This is much the same proportion that has been reported by other authors in series of cicatricial cancers.[13,14,16] It shows a higher proportion of males than do the unselected series of skin cancers and this is much as one might expect if such things as occupational hazards are considered.[17-19] However, it would be difficult to explain on the basis of exposure.

The pattern of age in relation to the specific problem of trauma is not different in the over-all series from that reported by other authors. The chronic trauma group forms a slightly younger section than the acute group. Of the chronic group 20% were in their forties and 22.6% in their fifties. This is a slight shift to the left (Table 6).

The basic nature of the injury for the total group is shown in table 7. Thirty-one of the 36 lacerations are in Groups I and II. Fifteen of the 18 burns and all of the more chronic processes are in Group III. These are essentially the same as reported by other authors. It is interesting that Pack and Treves[16] describe an acute burn cancer. We have one in-

TABLE 5

LOCATION OF CARCINOMA

	Scalp	*Trunk*	*Extremity*	*Face and Neck*
Group I (1-12 mos.)	1	0	7	5
Group II (12-120 mos.)	0	0	16	16
Group III (120 mos. +)	6	4	14	7
Total	7	4	27	28

TABLE 6

CICATRICIAL CARCINOMA (10 Years +)
DISTRIBUTION BY DECADES OF LIFE AT TIME OF DIAGNOSIS

Age	*No.*
10-19	2
20-29	2
30-39	1
40-49	6
50-59	7
60-69	8
70-79	4
80 +	1

TABLE 7

SOURCE OF ORIGINAL INJURY
(Total Group)

Laceration	36
Burn	18
Chronic draining sites	9
Frostbite	2
Stasis ulcer	1

stance of an acute cancer. This developed within 5 months of the burn and there were 2 other cases with latent period of an average of 42 months.

The skin cancers in this series were dominantly squamous and this is in keeping with the experience of Lawrence[13] in his series of cicatricial cancers.

Conclusions

We believe it has been adequately established that there is a significant relationship between long-standing cicatrix and secondary injury resulting in epithelioma of the "Marjolin" type. The nature of this relationship has been reviewed and the experimental evidence surveyed which may shed some light on this problem. Whether this same series of events may take place with a short latent or lapse period in the so-called acute trauma type of epithelioma is debatable. The study of the relatively small series of cases from the Vanderbilt University Hospital leads us to believe that through the "promoting" agent and "initiating" agent as a series of events there may actually be a cause and effect relationship between trauma and cancer. This is substantiated in some to some extent by the variation in microscopic character, location of the tumor, and sex distribution of patients in the Vanderbilt University series. In the instance of cicatricial cancers of the Marjolin type there is no reasonable doubt that these are capable of spread by both lymphatic routes and through the blood stream in some instances. They do not represent some bland variant of carcinoma *in situ* and should be treated vigorously by adequate extirpation and, where applicable, by concomitant dissections of the lymph node.

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Discussion (Abstract)

Dr. Robert E. Lyons, San Antonio, Tex. Dr. Byrd and his associates, by analyzing records of the Vanderbilt University Hospital, have shown once again that trauma can promote the appearance of carcinoma of the skin.

Dermatologists agree that there is a tendency for carcinoma of the skin (usually of the squamous variety) to develop in pathologic processes such as chronic burns, actinic dermatitis, chronic ulcers and sinuses, leukoplakia, keratoses, nevi, etc. These we refer to as precancerous dermatoses. Whether the development of carcinoma in chronic lesions require acute trauma or not is academic. Dr. Byrd has done us a great service by re-emphasizing that carcinoma, usually of the squamous variety, can and does arise in pre-existing lesions and that, at times, they are of a most malignant variety, necessitating radical treatment.

My only disagreement with Dr. Byrd is nosologic. I believe we should reserve the term traumatic carcinoma for those arising within a short period of time on otherwise normal skin following a wound, incision, laceration, stab, gash, puncture, abrasion or other injury. Those arising on precancerous dermatoses should not be classified as traumatic but rather as a neoplasm secondary to the pre-existing pathological process.

Dr. Byrd has doubted that bona fide cases of acute traumatic carcinoma occur. I believe that the strict application of Shields Warren's criteria in proving trauma as causative in carcinoma of the skin would surely and radically reduce the number claimed in the literature. These criteria include proof: (1) that the skin site was normal prior to the injury; (2) that the injury was severe enough to disrupt tissue continuity; (3) that the carcinoma arose soon after the injury; and (4) that the cancer was the result of repair and regeneration of the tissue injured. If cases of carcinoma of

the skin follow acute trauma at all, Gardner's theory of the role played by injury is most plausible (Gardner, A. W.: Trauma and Squamous Skin Cancer, Lancet 1:760, 1959). He states that trauma is a co-carcinogenic stimulus, i.e., a stimulus which of itself cannot produce a cancer but will accelerate, promote or bring to fruition the appearance of a cancer in a cell in which the initiation of a cancer had been produced by a carcinogen (or initiator). This theory could as easily explain the pathogenesis of a neoplasm arising in one of the precancerous dermatoses, where the pathologic process itself is the carcinogen and injury, applied acutely or over a long period of time, the co-carcinogenic stimulus.

I would like to emphasize that a high index of suspicion, when dealing with long standing cases of the precancerous dermatoses, will result in early diagnosis of the cancers forming therein.

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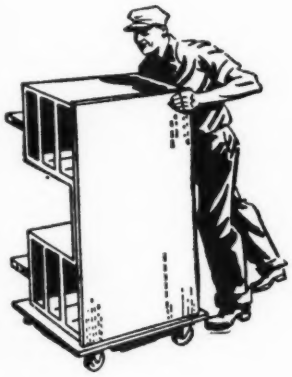

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CASE REPORT

Saint's Triad

WILLIAM F. BARRY, JR., M.D., R. W. POSTLETHWAIT, M.D., and CHARLES L. NANCE, M.D.,† *Durham, N. C.*

SAINT'S TRIAD is a term applied by Muller[1] to those patients with cholelithiasis, hiatal hernia, and colonic diverticula. Muller had observed 3 such patients within a period of 6 months and believed this frequency to be too high for coincidence. Palmer,[2] in 1951, reported 5 examples in a series of 31 cases of hiatal hernia and later[3] described 24 cases in 170 patients with hiatal hernia, an incidence of 14 per cent. Sixteen other cases had been reported to this time.[4-6] Three more patients with Saint's triad are described below; one also had an associated pharyngo-esophageal diverticulum.

FIG. 1

Case 1. A 63 year old white man was admitted in 1958 with a history of many years of constipation. Hemorrhoidectomy had been performed in 1916 and 1924. In 1952, he experienced a massive gastrointestinal hemorrhage at which time he was said to have a gastric ulcer demonstrated radiographically. In 1953, he was found to have cholelithiasis and diverticulosis of the colon. In 1955, a hiatal hernia was demonstrated. His only symptom is constipation. (Figs. 1-3).

Case 2. A 67 year old white man was admitted in 1952 with a history of constipation for many years. For

FIG. 2

†From the Departments of Radiology and Surgery, Duke University Medical Center, Durham, N. C.

FIG. 3

several days he had been passing bright red blood in his stools. He had no other symptoms. A pharyngo-esophageal diverticulum, hiatal hernia, cholelithiasis, and diverticulitis of the sigmoid colon were found (Figs. 4-6). The diverticulitis was thought to be the cause of the melena. He responded to medical treatment and refused surgery.

Case 3. A 61 year old white woman was admitted in 1960. For years she had had intermittent epigastric and right upper quadrant pain lasting a few hours and followed by residual soreness in the right upper quadrant for several days. The last attack was more severe than the others and was accompanied by nausea and vomiting. Substernal radiation of pain with a burning sensation had occasionally been noted. Cholecystectomy was performed for calculous cholecystitis. Her symptoms recurred, however, about 4 months after operation. Studies now demonstrated a hiatal hernia and a diverticulum of the colon (Figs. 7-9).

FIG. 4

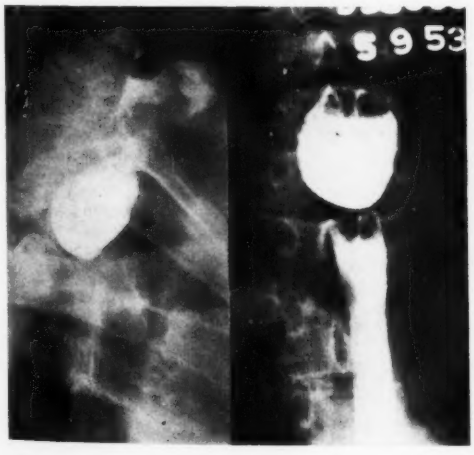

FIG. 5

Discussion

The exact incidence of this triad at this hospital cannot be given. During a period of one year (1958), 437 cholecystograms and 2,063

FIG. 6

FIG. 7

gastrointestinal studies were performed. A review of the films on these patients failed to disclose an additional example of Saint's triad. A 5 year review of the diagnostic index of all cases having any one of the three lesions also added no cases. The incidence here, therefore, is considerably less than that noted by Palmer.[3]

Muller, in seeking a common etiologic factor to explain this triad, suggested that obesity and chronic constipation may cause the diverticula and hiatal hernia; the resultant "stasis" then leads to infection of the biliary tract and gallstones. We believe, however, that the association of these three entities is much more likely to be on the basis of coincidence. The description of the triad does indicate the necessity of careful evaluation of symptomatology to avoid unnecessary surgical procedures.

FIG. 8

FIG. 9

Summary

Saint's triad, consisting of hiatal hernia, cholelithiasis, and colonic diverticulosis, is considered coincident, but does direct attention to the need for careful studies in patients with obscure gastrointestinal complaints.

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Effects of Chlordiazepoxide in Psychiatric Disorders*

IRVIN M. COHEN, M.D., *Houston, Tex.*, and
TITUS H. HARRIS, M.D.,† *Galveston, Tex.*

From an uncontrolled study of the use of this drug the authors believe it has a place in the treatment of anxiety, mild depression and phobias. It has certain untoward by-effects which are emphasized by the discussant.

CHLORDIAZEPOXIDE (Librium) is a new psychosedative chemically unrelated to any known psychotropic drug. Randall and co-workers[1] demonstrated in animals that in many respects it is qualitatively similar to meprobamate as a tranquilizer but is considerably more potent. This greater potency results in an extended range of therapeutic action and consequently broader clinical applicability. It has also been shown to possess certain unique therapeutic properties in addition to its attributes as a tension reducing agent.[2-4]

Our study was undertaken to further assess the therapeutic value of chlordiazepoxide in various psychiatric disorders and to identify specific psychopathologic symptoms responsive to it. Conclusions were drawn from the pooled results of two investigators treating independent groups of patients in separate treatment settings. We found that chlordiazepoxide is an effective and safe drug for controlling various psychoneurotic symptoms, that it is of limited value in the treatment of disturbed psychotic patients, and that it may be useful in reducing the intensity of phobic and obsessive ideation.

Pharmacology

Chlordiazepoxide is 7-chloro-2-methylamino-5-phenyl-3H-1, 4-benzodiazepine 4-oxide hydrochloride. In vicious animals it exerts marked "taming" action. That is, it calms without reducing alertness or locomotor ability. In contrast, the doses of meprobamate, chlorpromazine, and phenobarbital necessary to reduce the ferociousness of monkeys, for example, inhibit motor activity or produce ataxia.[1] It is twice as potent as meprobamate in producing muscular relaxation and approximately ten times as active in blocking the spinal flexor response. Other effects include appetite stimulation, anticonvulsant activity, and slight anti-inflammatory and analgesic effects. It has weak vasodepressor activity, no ganglionic blocking properties, and a low level of toxicity.

Material and Method

The study was designed as an extensive clinical trial without external controls. Improvement was estimated by clinical observation and subjective reports of patients. Improvement was graded as follows: (1) markedly improved—disappearance or marked reduction in intensity of symptoms; (2) moderately improved—appreciable relief but with some persistent discomfort; (3) unimproved—no change or worsened. The series consisted of 132 private inpatients and outpatients of whom 50 were males and 82 females. Ages ranged from 15 to 73. Examinations of physical and mental status, routine hemotologic studies, and urinalyses were done prior to instituting treatment. The drug was administered for periods up to 7 months. Target symptoms included tension, anxiety, rage, depression, phobias, obsessions, compulsions, psychophysiologic symptoms, paranoid delusions, and auditory hallucinations. Included in the series were psychoneurotic reactions, psychophysiologic reactions, personality disorders, affective reactions, and schizophrenic reactions. Distribution of target symptoms and drug response is tabulated in table 1. Diagnostic distribution and drug response is tabulated in table 2.

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†From the Department of Psychiatry and Neurology, University of Texas Medical Branch, Galveston, Tex.

TABLE 1

SYMPTOM DISTRIBUTION AND DRUG RESPONSE

Symptom	*Number of Patients*	*Markedly Improved*	*Moderately Improved*	*Unimproved*
Tension and anxiety	108	57 (53%)	28 (26%)	23 (21%)
Psychophysiologic symptoms	32	14 (44%)	8 (25%)	10 (31%)
Depression	50	18 (36%)	2 (4%)	30 (60%)
Rage	3	2 (66%)	0	1 (34%)
Phobias	10	8 (80%)	2 (20%)	0
Obsessions	18	10 (56%)	5 (28%)	3 (16%)
Compulsions	8	2 (25%)	3 (37%)	3 (38%)
Paranoid delusions	4	0	0	4 (100%)
Auditory hallucinations	2	0	0	2 (100%)

Results

(a) *Clinical pharmacologic actions:* The action of chlordiazepoxide resembled that of tranquilizers in that therapeutic effect occurred without clinically detectable clouding of consciousness or impairment of intellectual acuity. Two types of therapeutic action were observed. The most frequent was *calming,* producing relaxation and reduction of tension. The second was *stimulation,* which occurred in 15% of cases. This type of response was characterized by mild euphoria and increased urge for activity, effort, and socialization. It was unaccompanied by motor restlessness or insomnia, such as may result from amphetamines, or signs of drug intoxication. The reaction was unlike any produced by other psychotropic drugs with which the investigators were familiar and was desirable from a therapeutic standpoint. However, in 34% it disappeared in approximately 3 weeks and could not be reproduced either by increasing dosage or continuing the drug. In such instances the presenting symptoms usually recurred but with reduced intensity. Subsequent response to chlordiazepoxide was generally poor.

TABLE 2

DIAGNOSTIC DISTRIBUTION AND DRUG RESPONSE

Diagnosis	*Number of Patients*	*Markedly Improved*	*Moderately Improved*	*Unimproved*
Anxiety reactions	46	32	4	10
Psychophysiologic reactions	15	8	2	5
Affective reactions	41	10	18	13
Phobic-obsessional states	10	8	2	0
Obsessive-compulsive reactions	8	2	3	3
Schizophrenia	7	1	2	4
Personality disorders	5	2	1	2
Total	132	63 (48%)	32 (24%)	37 (28%)

Marked stimulation of appetite with excessive weight gain reported by others[2,5] was occasionally observed in this series. Antidepressant effects were also noted and will be discussed below.

(b) *Symptom response*: Uninterrupted administration for 24 to 72 hours was usually required for maximal response to a particular dosage level. Symptomatic relief, either temporary or prolonged, was derived by 72% of patients regardless of diagnosis. Tension and anxiety were identified as the symptoms most likely to respond to chlordiazepoxide, especially if they were the presenting symptoms. Thus, improvement was obtained in 79% of patients complaining of nervousness, vague feelings of unrest, feelings of impending disaster, and similar indicators of free floating anxiety. Anxiety of mild to moderately severe levels responded well, but extreme anxiety, as seen in panic reactions, did not respond as regularly. Of 4 patients having neurotic anxiety of panic proportions, one was markedly improved, one was moderately improved, and 2 derived no benefit. Four agitated schizophrenics failed to respond to chlordiazepoxide but reacted favorably to injections of chlorpromazine. Psychophysiologic symptoms, especially gastrointestinal, also responded well, particularly when accompanied by tension and anxiety.

Antidepressant properties were observed. Also, the stimulant action of this drug occurred with greatest frequency in depressed patients. The class of depressions most frequently improved were those reactive to situational problems. Endogenous depressions responded less frequently and less satisfactorily, and no patient in this series having a severe mood disturbance derived appreciable im-

provement on the doses of chlordiazepoxide used in this study.

Unexpected benefits occurred in patients having phobias, obsessions, and compulsions, symptoms notably unresponsive to drug therapy. Although these patients received intensive psychotherapy and chlordiazepoxide simultaneously, speed of improvement was more rapid than is ordinarily expected from psychotherapy alone. Ten patients presenting phobic and obsessive thinking improved on chlordiazepoxide. Eight were females with relatively brief histories of obsessive thoughts of infanticide and phobias of remaining alone, one was a woman with a history of 8 years of infanticidal obsessions and a phobia of driving in unpopulated areas, and one was a man with obsessive thoughts of homicide for 6 months. Significant improvement occurred in all these patients in from one to three weeks. Eight patients were typical obsessive-compulsive psychoneurotics. Disabling symptoms were modified in 5 after starting chlordiazepoxide. Six months later 2 showed sustained improvement while on maintenance doses, one periodically had worsened despite maintenance doses but felt generally better, and 2 patients no longer responded to the drug.

Paranoid delusions in 4 patients and auditory hallucinations in 2 were unaffected by the drug. These patients were also verbally aggressive and agitated but none responded to maximum daily oral dosages of 140 mg.

(c) *Diagnosis response*: Psychoneuroses, particularly anxiety states, responded most favorably. If anxiety was somatized, as in psychophysiologic reactions, the rate of improvement was slightly lower. Our sample of schizophrenia was too small to derive definitive conclusions but it was our impression that bizarre schizophrenic ideation was unaffected by this drug. However, it did appear to have some applicability in the treatment of neurotic symptoms appearing in pseudoneurotic schizophrenia. The sample of personality disorders was also too small to allow decisive conclusions. Of the 5 cases in which marked improvement was obtained the predominating symptom was periodic rage. In all cases the underlying psychopathology remained unchanged. Our final conclusion was that chlordiazepoxide is a symptom relieving drug having no specific diagnostic indications.

Dosage

The most frequently effective dosage was 10 mg. t.i.d. However, no reliable criteria could be found to forecast adequate dosage. Neither intensity of symptoms nor body weight relationship were significant determinants. Individualization of dosage was therefore required. Once a therapeutic level was reached it was generally unnecessary to alter dosage throughout the course of treatment. Experience proved that if symptoms were not ameliorated within 3 to 7 days after a starting dose of 10 mg. t.i.d., the dosage should be progressively increased to the point of therapeutic effectiveness or appearance of ataxia which is a sign of overdosage. Continued administration was generally fruitless if ataxic levels were reached without signs of improvement. The maximum effective dosage was usually 20 to 25 mg. t.i.d.-q.i.d. The possibility of a cumulative effect was suspected in a few cases by virtue of sustained improvement despite lowered dosage, and in others by the sudden appearance of toxic effects after periods of relative freedom. Such signs appeared mainly in patients receiving dosages exceeding 40 mg. daily. Elderly patients as a group tolerated only small dosages, usually 10 mg. b.i.d.

Side-Effects and Complications

Drowsiness and ataxia were the chief side-effects. They were directly related to dosage or individual sensitivity and could be quickly abolished by decreasing total daily dosage. However, they rarely occurred in the most generally applicable dosage range of 10 mg. t.i.d.-q.i.d. Greatest incidence was in patients receiving 100 mg. daily or higher. Geriatric patients were particularly sensitive, often experiencing side-effects without obtaining therapeutic benefits. Side-effects appeared in sensitive patients within 24 to 36 hours. However, in most cases they appeared on the third or fourth day and occasionally as late as the seventh. Gait disturbances ranged from occasional unsteadiness to gross ataxia. Irritability, overassertiveness, and hostility were observed in 0.5 per cent. Two geriatric patients with organic brain disease and agitation not included in this series developed dysarthria and dysphagia, their clinical pic-

tures resembling pseudobulbar palsy. Alcohol appeared to potentiate the effect of chlordiazepoxide, this impression being drawn from the fact that several patients became grossly ataxic while only mildly intoxicated.

No side-effects referable to the cardiovascular, gastrointestinal, or autonomic nervous systems were observed. No extrapyramidal complications occurred. No hemopoietic, renal, or hepatic abnormalities took place. None showed impairment of intellectual functions. Dependence and addiction have not been observed to date, and abrupt withdrawal produced no ill effects.

Summary and Discussion

The results of our study confirm earlier reports of the effectiveness of chlordiazepoxide against a variety of psychopathologic symptoms. It is useful in the management and treatment of anxiety, psychophysiologic symptoms, mild depressive affect, phobias, and obsessive ideation. Its most potent action is against a wide span of anxiety and tension. Comparative studies were not made but it is our impression that chlordiazepoxide exerts calming action beyond the limits of meprobamate and approaches that of the phenothiazines. It is a symptomatic drug capable of producing relief mainly in psychoneurotic reactions. Its utility in psychotic reactions, particularly schizophrenia, appears to be low but this needs further study, particularly utilizing higher dosages.

At the most widely applicable dosage level chlordiazepoxide is virtually atoxic. Since its most common undesirable effects, drowsiness and ataxia, can be abolished merely by decreasing dosage, such effects probably should be regarded as signs of overdosing rather than true side actions. Our findings indicate that it is unnecessary to administer doses producing ataxia to achieve satisfactory therapeutic results. Also, reducing dosage to eliminate undesirable effects does not impair the drug's effectiveness. Finally, dosage must be tailored to the needs of the individual patient.

Serious complications were notably absent in this series. Psychomotor hyperactivity and acute rage reactions reported by others[2] did not occur in this series but may be elaborations of the hyperirritability we occasionally observed. Smith[6] described "extrapyramidal stimulation" in schizophrenic patients receiving doses above 400 mg. daily but unfortunately did not describe the effect and his terminology was not defined more explicitly. His report is the first to suggest that chlordiazepoxide may have extrapyramidal effects.

The evidence is strongly suggestive that this drug exerts selective action on certain types of psychogenic symptoms. However, it is possible that relief may be the result of merely nonspecific blockade of tension, specific symptoms diminishing as the anxiety which reinforces them subsides. The multiple clinical actions of chlordiazepoxide complicate explanation of its site and mode of pharmacologic activity. The paradoxical effects of stimulation and sedation, coupled in some patients with heightening of appetite, suggest effects on the reticular system and its hypothalamic connections. The similarity of these actions to those of monamine oxidase inhibitors implies the possibility of effects on serotonin and/or norepinephrine metabolism. An alternative explanation is that chlordiazepoxide produces sedation at one brain level and stimulation at another. Finally, the absence of extrapyramidal complications implies a site and mode of action different from the rauwolfia alkaloids and phenothiazine derivatives.

Conclusions

1. Chlordiazepoxide is a useful and safe drug in the management and treatment of anxiety, psychophysiologic symptoms, mildly depressed moods, phobias, and obsessive thoughts.

2. Drug response is in the form of either sedation or stimulation.

3. Chlordiazepoxide is a symptom-relieving drug having no specific diagnostic indications.

4. Ataxia, its most common undesirable effect, can be promptly abolished by reducing dosage.

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Discussion (Abstract)

Dr. Neville Murray, San Antonio, Tex. In discussing this interesting paper on the effects of chlordiazepoxide in psychiatric disorders by Drs. Harris and Cohen, I should like to contrast their impressions of this substance upon their patients with my own group of patients, whose unpredictable reactions have impressed me with the potency of this substance. The necessity for close care and observation in those persons taking this substance by a competent neuropsychiatrist appears mandatory. I choose the word neuropsychiatrist purposely, since there are apparently both neurologic and psychopathologic involvements in response to methaminodiazepoxide. The fact that the manufacturers of the substance have given it the trade name of "Librium" should not be overlooked. This name was chosen to record the antagonistic effects to equilibrium. Presumably since "Disequilibrium" would hardly be a marketable brand name, the shorter and more ambiguous "Librium" has been preferred. Nevertheless, what is described by the authors of this paper as an occasional ataxia reaches significant proportions insidiously and cumulatively in patients taking doses as small as 30 mg. a day over a period of time. In 2 such patients under my care, one taking 30 mg. of the drug daily, the other 50 mg. daily, on being subjected to depth perception tests, utilizing the Howard Dolman test, the one on 50 mg. a day on the first testing showed readings of —4, —4, —3 and on the second comparative readings, 7 days after stopping the drug, plus .5, —2, —.5 with a Maddox Rod muscle testing response of abnormal on first test. After 7 days' freedom from the drug substance, the patient showed a normal response to Maddox Rod. The other patient on a 30 mg. daily dosage showed on the first test —3, —.5, —2.5, and on the second test 7 days off Librium showed responses of —1, plus 1, —1.5, again showing a change from borderline normal to normal. Maddox Rod muscle testing test showed similar changes from borderline to normal. Pre-existent phobias appeared to be exaggerated by the ingestion of chlordiazepoxide. These tests were carried out as a result of the involvement of both people in driving difficulties. I have previously reported that in a 90 day period, out of 68 drivers taking Librium in daily dosages from 10 to 100 mg. daily, 10 were involved in minor and 6 in major road accidents, showing a tenfold increase in the projected statistics provided by the Texas Highway Department. These highway accidents were peculiar insofar as patients involved appeared to be the injured parties, rather than the injurious. They were not necessarily preceded by evidence of cerebellar ataxia.

One of my patients, a psychologist, noted a rather subtle but nevertheless significant change in his driving habits on a dosage of 30 mg. of Librium a day over a 60-day period. He found that there had been a change in his ability to study the instruments of his car which he normally did in a rather compulsive manner, and maintain a memory image of the pattern of the traffic on the road ahead of him. Thus when he brought his eyes up to view the traffic situation as it had developed in his brief absence he was, he reported, "surprised" by the configuration which he encountered and realized to his dismay that he had evidently not been paying sufficient attention prior to the time that he took his gaze off the road. Robbed of his "tonic" anxiety he had not cared sufficiently about the activities of his fellow road-users and thus was robbed of his capacity to anticipate their behavior.

This is not a side-effect of chlordiazepoxide but an "effect" of the drug—the diminution of anxiety. We are then faced with the dilemma as to whether or not it is desirable as physicians to rob our patients of their normal protective reflexes or behavior patterns, in order to ameliorate them from the distress of their episodic hyper-reactivity. We should never attempt to suppress the symptom presented by a patient until such time as we are willing to examine and deal with its origins. Merely to place a psychologic plaster cast on a fractured personality function to be left indefinitely, without examining the nature, extent, or therapeutic progress of the injured member is to do patients poor service. What is said here is likely to be spread abroad and if we are to harbinger the impression that methaminodiazepoxide is an ideal and completely safe "symptom suppressor" it will be used and abused by those members of our profession not necessarily intent upon examining the origins of their patients' psychologic difficulties and helping them to deal with them, but rather to have them conform to a superficially bland and conformist way of life. In so doing they may be denied the benefits of their own protective defense mechanisms found by natural process.

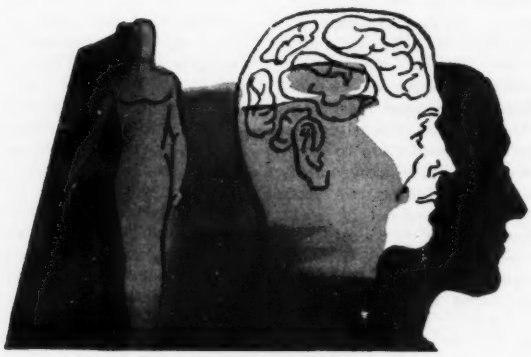
Certainly chlordiazepoxide would appear to be one of the most potent and interesting substances to come to hand in recent years in terms of its capacities to exert an "anti-repressant" effect upon those people taking it in sufficient doses. The question of individual dosage appears to be very closely parallel to the capacity to metabolize alcohol, to which it has certain likeness both in its pharmacologic as well as in its psychologic effects. Just as some people get "happy-drunk" and some "sad-drunk," there are those who become hypomanic and excited and others who become depressed and retarded in response to the effects of Librium. Both substances cause an incapacity to coordinate cerebellar function. Alcohol would appear to have some advantages: it tastes better, is less expensive to buy, and is more rapidly metabolized. Certainly it is more universally employed. I am reminded of one of the salesmen for Hoffmann-La Roche who indicated with great glee that he thought his product was as good as a Martini without the olive.

And so it may be said that if you drink, don't drive —if you take Librium, be careful when you drive. Any substance which is apt to relieve the patient of his tonic protective anxiety and interrupt his capacity to reflexly coordinate his cerebellar activities must be handled with exceeding caution in contrast to the haphazard empirical and palliative fashion in which its use is commonly encouraged at present.

I should like to ask the authors whether or not they had noted any significant changes in the driving habits of their patients. Those patients treated while

in hospitals would not be likely to have any automobile difficulties and, strangely enough, only about 60 to 70% of people who suffer from nervous trouble ever drive an automobile at any time. Certainly, unless the questions are specifically asked of the patient, they are not likely to volunteer the apparently trivial and irrelevant details of traffic accidents. I should also like to ask the authors whether or not any of their patients suffered injuries due to the falls that occurred as a result of the ataxia. These falls seem to have a particularly sudden kinetic and incoordinative characteristic about them. Some 4 of my group of patients have suffered bony injury as a result of them; one a fracture of the femur in a 55 year old woman. I would like to further recommend the use of the modification of the Romberg test to note dysequilibrium when the patient is asked to close his eyes and nod his head up and down in an affirmative gesture five or six times and then to come to rest with the eyes remaining closed and maintain an upright position. Then the patient is asked to move the head in a negative gesture from side to side a similar number of times and once more coming to rest in a face-forward position with the eyes closed, it is then that dysequilibrium is most likely to occur. Patients should be interrogated as to whether they bump into doorways or bump into furniture around the home, as to whether or not they have any difficulty in holding objects or conducting skilled movements such as playing the piano, typing, or others involving rapid coordinative successive movements.

I agree with the authors as to the value of this substance, as to its interest, and as to its potency. I submit, however, that it should be used only by those people competent to deal entirely with the origins of the symptoms for which it is administered and, second, I feel that patients who take this substance should be cautioned and closely observed for the undesirable effects of this substance in terms of antirepressant and neuropathological activity.



Radiation—Industry's Best Understood Problem*

J. A. QUIGLEY, M.D., *Cincinnati, Ohio*

The author emphasizes the accurate means by which radiation hazards may be spotted. He indicates the good record established by the industries processing uranium, for example.

Introduction

RADIATION and the handling of radioactive materials is not new to the medical profession. Each of you in your premedical and medical school training learned the basic principles of radiation. Despite the reports in the lay and scientific press, these principles have not changed.

The effect which radiation has on the body depends upon its ability to produce ionization in or near the individual cells of the body. If only a small amount of ionization occurs, there may be only slight change. However, if there is sufficient ionization, the individual cell may be seriously damaged or completely destroyed. If only a few cells are involved, there may be no clinical evidence of damage. If many cells are involved, there may be permanent local injury; or if the whole body is involved, it may result in any of the varying degrees of radiation sickness up to death of the individual.

The important points are: the area of the dose (local or general), the total dose, and the dose rate.

For over 60 years there has been an ever-increasing use of radiation-producing devices and materials in medicine. During these years we have learned the hazards associated with radiation and the methods of protecting ourselves and our patients against these hazards. This knowledge was not acquired without cost. Some physicians were seriously injured in the early days. By and large, however, the price that was paid for our present knowledge has been greatly exaggerated.

Standards for exposure to radiation were developed before 1930. I think it is most important for all of us to remember that at no time has there been evidence of injury where these standards were followed. These standards were established for the most part by physicians. Because of their knowledge in the field, in the early days of the Manhattan Project, forerunner of the Atomic Energy Commission, physicians were called upon to assist in the establishment of radiation standards for those who were to work on this important project. Their advice was heeded and the record proves the adequacy of the standards that were established.

Despite this record, radiation exposure standards have been successively reduced. As an example, the maximum permissible dose of x- or gamma radiation has been reduced from 60 to 30 to 15 and most recently to 5 rads per year. This has been done despite the fact that no evidence of injury was ever seen, even at the largest dose level. These changes in permissible dose levels have greatly confused the general public and have, in fact, confused many physicians.

Since World War II matters of health protection against radiation and radioactive materials have been confused by politics and emotion. The political aspects have been on an international basis. Some of the emotional aspects have been provided by pacifists who could probably have better directed their activities in other fields. We in the medical profession may be subject to some criticism, since few physicians have been interested in the establishment of standards for radiation protection in recent years. The health physicists and others have taken over the field and have—as one of their own members has publicly stated—adopted an ivory tower approach.

Many experiments, especially at high levels of radiation dose, have indicated that radiation can be harmful. This is not new to us in

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medicine, since for years we have used radiation to kill tumor cells. On the other hand, at low levels many experiments have indicated a beneficial effect. Those presently in the field, however, have become so impressed by the harmful effects that they seem only to be able to report on deleterious effects. This is so much so that last spring at the hearings before the Joint Congressional Committee on Atomic Energy, a positive finding at low doses involving animals which outlived their controls was reported as "a negative deleterious effect."

Such an attitude, in my opinion, will delay the development of this country's full potential in the field of nuclear energy. Every scientific advancement has been associated with some degree of risk. There has always been a price. Development in this field will definitely be delayed—if not halted—if the attitude of "zero risk" prevails.

In June of 1956 the National Academy of Sciences—National Research Council issued their famous (or infamous) publication, "The Biological Effects of Atomic Radiation." The chapter by the geneticists was quoted and misquoted in both lay and scientific publications. This section got world-wide publicity. However, in the section devoted to the report of the Committee on Pathologic Effects the following statement is made:

"Despite the existing gaps in our knowledge, it is abundantly clear that radiation is by far the best understood environmental hazard. The increasing contamination of the atmosphere with potential carcinogens, the widespread use of many new and powerful drugs in medicine and chemical agents in industry, emphasize the need for vigilance over the entire environment. Only with regard to radiation has there been determination to minimize the risk at any cost."

I would like to repeat the first sentence of that quotation: "Despite the existing gaps in our knowledge, it is abundantly clear that radiation is by *far* the *best understood* environmental hazard."

This is not to say that there is no hazard associated with radiation or with the handling of radioactive material, but I believe that it is still the best understood hazard. The most recent publication of the National Academy of Sciences—National Research Council, which I received only last week, again includes the above statement.

It would be impossible at one session to discuss all the aspects of the nuclear energy industry. The problems of the whole industry differ only in degree. In the operation of reactors we are dealing with very high levels of radiation. In the reprocessing of irradiated fuel elements, chemical separations are carried out on material which is very radioactive and which contains fission products. The isotopes used in medicine are basically internal emitters.

The operation of reactors to develop power is the largest single, peaceful use of nuclear energy. This field is expanding and will continue to expand. All the reactors in this country depend upon uranium or enriched uranium for their operation. Today we will confine our remarks to the health problems associated with the processing of uranium for reactors.

The basic problems are four in number: (1) external radiation, (2) internal emitters (airborne radioactive material or ingested material), (3) chemical hazards, and (4) other hazards.

External Radiation

For practical purposes, we can divide external radiation into two types: (a) penetrating radiation, as for example, neutrons, gamma rays, and high-voltage x-rays, which penetrate deep into the body; and (b) soft or relatively nonpenetrating radiation, as for example, alpha, most beta particles, and some x-rays, which can penetrate only the superficial layers of the body at the most.

To understand the action of external radiation, we can best compare it with light or possibly with ultraviolet light. The source may be at varying distances from the body. Its effect on the body will depend upon the distance and upon the intensity of the radiation.

It is presumed that the LD-50 for humans to external penetrating radiation is somewhere between 400 and 600 r. We must remember, however, that where the dose rate is low, injury and recovery will both take place, at least in the somatic tissues of the body. It is probably impossible to detect any changes in the body from a whole-body dose of less than 25 r. In fact, whole-body exposures of 100 r will produce radiation sickness in only about 10% of the individuals.

As stated earlier, the maximum permissible dose for external penetrating radiation is 5 rads per year. From the uranium mines

through all the processing plants up to the production of reactor fuel elements, we do not have serious difficulties in operating at or below the maximum permissible dose for external penetrating radiation. At one time foreign ores received in this country contained a relatively large amount of radium. This did present an external radiation problem. At that time the maximum permissible dose (mpd) was 15 rads per year. It was not difficult, however, to operate at levels below the present mpd of 5 rads per year.

The maximum permissible dose for soft or relatively nonpenetrating radiation is 30 rads per year. This level does not present a serious problem in the uranium industry. Where it has been identified as a problem, it is not a serious one. Corrective measures are relatively simple.

Methods of Measurements. In the field of external radiation there are precise and simple methods of evaluating the problem. Portable ionization chambers and GM (Geiger-Müeller) instruments with a high degree of precision are abundant on the market. They are very simple to use, and in a relatively short time a high school graduate can be trained to make measurements of both penetrating and soft radiation. The survey instruments can be used for locating various sources of external radiation in a production area.

In addition to this equipment, film badges may be worn by each individual who is exposed to external radiation. The film badges, supplemented occasionally by pocket dosimeters, can be used to develop reliable records of exposure of each individual.

In addition to these methods of measurement, where high dose levels are possible, monitoring devices connected to alarm systems can be placed in the production area. We can therefore detect and warn against high-level radiation doses. We can determine after-the-fact the dose that each individual received, and we can examine the production area for day-to-day and job-to-job sources of external radiation. I know of no other environmental hazard where there is similar ease and accuracy of evaluation, both on a general and on an individual basis. Records of personal exposure, as outlined above, have been accepted in the compensation courts.

Protective Measures. All of us understand that as the intensity of light diminishes as we move farther from its source, so also does the intensity of a radiation dose, when the source is external to the body. In this case the density of the intervening air space provides shielding. By interposing any material of greater density than air between the source of radiation and the human body, the safe distance may be reduced. The greater the density of the interposing material, the greater may be the reduction in the safe distance from the source.

As you all know, lead is an ideal shielding material. Wood, water, steel and concrete also form excellent shielding materials. Uranium itself, because of its high density, is even better than lead as a shielding material. This at first may sound contradictory—using a radioactive material as a shield against a radioactive source. The density of uranium, however, is very high—18 to 13—as compared to lead. Because of self-absorption, when uranium is used as a shield, we have only to concern ourselves with the surface dose from the uranium, which is 240 mrads/hr. for beta and 5 mr/hr. for gamma. Since beta radiation is soft radiation, a very thin layer of steel will cut out almost all this dose. Given the intensity of an external radiation source, it is but a simple mathematical problem to determine the thickness of any shielding material which is necessary to create satisfactory working conditions in a given area.

Internal Emitters

The health problem in this case results from the deposit of radioactive material within the body. The mode of entry into the body is usually through the respiratory tract. Particles which are inhaled will be deposited along the respiratory tract or in the lungs. Particle size, of course, will determine the amount which will eventually reach the lung tissue. Larger particles are filtered out in the upper respiratory tract and may be removed by sneezing or coughing. Some of the material will be swallowed and absorbed from the digestive tract.

Of the material that reaches the lung tissue a relatively high percentage may be absorbed into the blood stream. Much depends upon the particle size and on the solubility of the particular compound. Interestingly enough, a relatively small percentage (up to 1%) of the material which reaches the digestive tract is absorbed.

Soluble materials especially will be absorbed into the blood stream and circulate throughout the body. A great deal of the material will

leave the blood stream by way of the kidneys. Some will be incorporated into new cells in both the bone and soft tissues. From these sites it will be slowly mobilized and again carried by the blood with a large factor excreted by the kidney.

Larger particles and relatively insoluble material which reaches the lung will find its way into the lymph system. Relatively large amounts of material may therefore become deposited in the lymph nodes in the hilar region of the lung. In the case of all internal emitters, such sources produce their effect on a 24 hour basis.

As in the case of external radiation, maximum allowable concentrations have been established for almost all radionuclides in breathing air. Actually, many installations in the uranium industry are operating at a level considerably below the present maximum allowable concentration. This has been done because the National Committee on Radiation Protection and Measurements has emphasized that the numbers appearing in the National Bureau of Standards handbooks should be looked upon as *maximum* and has recommended that operations be carried on as far below these levels as is practicable. Methods of measurement and engineering skills have been developed to a degree that makes lower levels obtainable. Actually, many uranium processing plants have adopted control standards one third to one fourth of the handbook values for uranium.

In all the processing steps of uranium—from mills to finished reactor fuel elements—control of airborne radioactive material is our most serious and interesting problem. In uranium mines this is not a serious problem, since the uranium content of the raw ore is relatively low. Uranium is always found in nature with some radium. The health problems in mines are from radon gas and exposure to silica. Controlling these problems will provide more than adequate control from the point of view of exposure to uranium.

Methods of Measurement. It is not at all difficult to measure the amount of radioactive material which becomes airborne. The precision of the methods of measurement, while not as great as in the case of external radiation, is still quite satisfactory. Air is drawn through a filtering media at a known rate for a predetermined period of time. The amount deposited on the filter media—usually filter paper—can then be readily determined by using standard counting technics. This is the basis of all the standard methods of determining the activity in the air. In some plants equipment is built in so that monitoring is done on a continuous basis. The filter papers can then be changed at regular intervals and good background data may be obtained.

Another method which is also in widespread use involves portable sampling equipment. This provides more detailed information on the exposure of an individual. Actually, two types of samples are taken by this method. The first of these is the "breathing zone" sample. In this case the industrial hygienist takes air samples in the breathing zone of the operator and times the various components of his over-all job assignment. "General air" samples and time evaluations must also be made in the vicinity of the man's particular place of work, smoking areas, rest areas, etc. From the information so obtained it is possible to arrive at a weighted daily exposure for each type of operation within a plant. It is also possible by this method to determine the particular operations which contribute the higher doses in the individual's over-all exposure. By sampling several operators on different shifts doing the same type of work, reliable exposure data may be accumulated.

At many sites a combination of the two methods described above is used.

In addition to the above, we can determine the urinary uranium output for each individual who is exposed. It is becoming more evident that the urinary output value may be roughly correlated with the weighted daily average exposure. In this connection the advisability of having a health team, which I shall discuss later, is well demonstrated. Regular meetings are held with the industrial physician, the industrial hygienist, and the head of the laboratory department to review urinary uranium outputs and exposure.

Protective Measures. Protective measures against airborne radioactive material should consist primarily of the removal of the material at its source of generation. This requires the application of adequate ventilation at all points where radioactive material may become airborne as a dust, mist or fume. Because of the comparatively low maximum allowable concentration for uranium in air, it is usually necessary to make extensive use of hoods and

enclosures over machines or to perform some operations in dry boxes.

In many cases elaborate exhaust ventilation and collecting systems are necessary. Such systems usually involve much more than exhaust systems designed for nuisance dusts. Because of the value of the material, it must be kept airborne from the source of generation until it reaches the dust collector. It is most important that the collecting system be maintained and operated at a high degree of efficiency.

Where the handling of radioactive materials is carried on, it is required that we know the amount of material released to the atmosphere. This makes it imperative that the exhaust gases from all dust collectors be monitored. Reliable methods of measuring stack losses have been developed. Because of the value of the material, the results of this sampling are very valuable to management from the point of view of accountability.

Other methods of controlling airborne radioactive material consist of the substitution of wet processes for dry ones wherever practical.

All types of dust respirators and airline respirators with both half- and full-face pieces are used. The shortcomings of such devices, however, must be recognized. If properly worn, both types of respirators can provide good protection. Each employee must understand the value of the respirator and must be trained in its proper use. In general, they should be looked upon as temporary solutions to be used only until adequate equipment may be designed and installed.

Of equal importance with the above protective measures is the training of the operators to do their work in such a manner as to cause the least amount of material to become airborne. An example of this is provided where a lathe is used to cut uranium metal. The chips which are produced are normally flushed by coolants into a reservoir at the bottom of the machine. Frequently, burning chips will hang up on parts of the equipment. As these chips burn, a large amount of fume and uranium oxides may become airborne. With adequate training the men may be taught to knock such chips into the reservoir where they will be promptly extinguished.

Chemical Hazards

It is important to remember that many radioactive materials may also have a toxic effect. Their action in the body from a toxic point of view will be the same as their nonradioactive isotopes. This is an important consideration in the handling of uranium which is a heavy metal and a nephrotoxin.

In addition to this, the processing of uranium involves the use of large quantities of acids—nitric, sulfuric, anhydrous hydrofluoric, hydrochloric, etc. These are normal problems in the chemical industry. They are no less serious in the uranium industry.

Other Hazards

The other health problems encountered in uranium processing are the everyday problems of all industry—thermal heat, high-voltage electricity, handling of materials, acids, caustics, etc. In the uranium industry special comment should be made about the handling of materials because of the density of the material. Hand and foot injuries are common. Fork lifts, which are widely used, also introduce their own hazards. It is these problems that keep medical departments and safety departments busy.

Special comment should also be made because of the pyrophoricity of uranium metal, especially when it is in fine form such as chips, turnings, sawdust, and grinder sludges. This is not just a safety problem, but is of great concern to the industrial hygienist and physician, since burning metal causes uranium metal fume and oxides to become airborne.

The whole industry of nuclear energy has an unusually good safety record. In 18 years only three deaths and a relatively small number of injuries can be attributed to radiation or the handling of radioactive materials. It has the usual problems of the chemical industry and metals production industries which have prevented the safety record from being even better.

As I stated at the outset, I believe that radiation is by far the best understood environmental hazard. I find it difficult to understand why there is so much concern about radiation and the handling of radioactive materials.

The Health Team

Occupational medicine has gone through three distinct phases. In the early days it consisted almost exclusively of the treating of accidents and occupational diseases. In the second phase emphasis was placed on early diagnosis. In this phase safety programs and pro-

grams of industrial hygiene really began to develop. In the third stage the emphasis has been on prevention. Prevention is not only the byword of industrial medicine, but it is also the goal of the industrial hygienist and the safety engineer.

These groups are not—or should not be—in competition. We are all interested in the health of people who work regardless of their position in the industrial organization. Yet, even today, in many companies the efforts of the three groups are poorly coordinated. Because of the administrative organization they sometimes actually appear to be in competition. Certainly it is not uncommon to see one or the other in a dominant position.

Occupational medicine has now achieved specialty status, with the objectives, functions, and scope of the specialty clearly defined. Occupational medicine in the nuclear energy industry can and does fit within this framework. Industrial hygiene has likewise become a specialty, the scope and functions of which are also clearly defined. Where radiation or the handling of radioactive materials is a problem, the well-trained industrial hygienist can understand and cope with this problem, too. In my opinion, the detection, measurement and correction of radiation problems is not essentially different from the detection, measurement and correction of other environmental hazards. I believe that there is no conflict between industrial hygiene and industrial medicine. Each should complement the other.

Both groups need the support of a well-trained analytical laboratory group. Such a group must be able to measure all effluents from the plant site, to analyze samples of the environment for all types of hazards including radiation, and to be able to do chemical analyses, as for example, uranium or radium in urine and other excreta.

The necessity for a good safety program is well understood by all, the safety engineers having been one of the first groups to define the scope and functions of their field. Working on a health team, safety engineers come to understand the problems of the industrial hygienist, including the radiation problems. In their plant inspections they learn to recognize deviations from accepted procedures. The industrial hygienists for their part come to understand the general field of safety, and as a result, both groups do a better over-all job.

Where the efforts of the four separate groups are coordinated into a health team, I believe the best results will be obtained. While the concept of the health team is not entirely new, I believe that it is one that will find broader application in industry in the future. The physician alone or the medical department alone, as we know them, is not in a position to cover all the aspects of a good preventive program.

This brings us to the logical question of who should head the health team. I do not believe it is necessary that the group be headed by a physician. I have seen more than one good health team headed by very capable industrial hygienists. I do, however, believe that it is more logical for a physician to head such a group. Physicians by training understand not only the medical aspects but have been well schooled in basic chemistry and physics. Certainly it is easier for a physician to understand the over-all problems than it is for a safety engineer, industrial hygienist, or laboratory chemist.

We, as physicians, must be willing to assume the responsibility and provide the leadership that is necessary to get the best team effort.

Summary

Physicians must take more interest in radiation and radiation standards. Standards must be reasonable and realistic. The problems of radiation are well understood, methods of measurement have been refined to a high degree, and preventive measures have proven adequate. The problems in the uranium industry are essentially the same as those of industry in general. The over-all problem is best handled in a health and safety division composed of separate departments of medicine, safety, industrial hygiene and chemistry. This will assure a balanced team effort. Physicians are the logical leaders of such a team, though in the last analysis this must be determined on the basis of merit.

Stapedectomy with Vein Graft for Deafness Due to Otosclerosis*

HARRY ZOLLER, M.D.,† *New Orleans, La.*

The author describes his results with this technic.

DEAFNESS due to fixation of the stapes was discovered by great otologists as early as 1735. Kessel in 1878, Boucheron in 1888, and Miot in 1890 mobilized the stapes with a resulting improvement in hearing. The operation had undergone several modifications and in 1899 this surgical approach was abandoned. In 1952, Rosen,[1] when palpating the stapes, obtained not only good mobilization of the stapes but also a resulting improvement in hearing. The mobilization of the stapes resulted in reankylosis and as a result varied procedures were introduced. Michel Portmann[2] of France and John Shea[3] of Memphis described fenestration of the oval window and substitution of a vein graft for the stapes footplate. Ossicular continuity was re-established by use of the stapes or a polyethylene strut.

The indications for stapes surgery will depend on the following conditions and the more selective one is in cases the higher the percentage of results: (1) There should be at least a 25 decibel air-bone gap in the speech frequency with a good speech discrimination score of 75% or better. (2) Bone conduction should be 40 decibels or better with a good air-bone gap. (3) Conductive losses with fixation of the stapes due to otosclerosis or adhesive otitis media.

The great percentage of improvements in hearing following stapes mobilizations receded because fractures often occurred through an otosclerotic focus with a resultant reactivation of new bone formation. Altmann and coworkers[4] proved, on specimens at autopsy, that with removal of the stapes and reconstruction of the ossicular chain there was a complete absence of serious labyrinthine reactions in those examined histologically. Anatomically the saccule and utricle are located far enough in the vestibule to permit cautious removal of the involved footplate.

In my last 30 cases of otosclerosis I have used the stapedectomy and vein graft technic of Shea. The patient is heavily sedated. Two hours preoperatively pentobarbital sodium (Nembutal) 0.1 to 0.2 Gm. is given followed by 75 mg. of meperidine HCl (Demerol) and 10 mg. of compazine 30 minutes before surgery.

The ear canal is prepared by irrigating with a soapy solution and followed by scrubbing the ear with soap, alcohol, and ether. The head is draped and positioned. Next, the hand is prepared with the same solutions and a vein graft about 6 mm. in length is removed and placed in Ringer's lactate solution.

Under a magnification of 10 times with the operating microscope a triangular incision is made in the posterior auditory canal about 8 to 10 mm. from the annulus. This skin flap is dissected out of the annulus and folded anteriorly. To obtain good visualization of the posterior crus of stapes and its footplate it is necessary to take down the necessary amount of the outer aditus wall with curettes. With magnification of 16 times one can now check the degree of fixation of the stapes and see the type of otosclerosis present (Fig. 1).

The stapedius tendon is divided followed by the separation of the incudostapedial joint. The stapes is then removed by doing an anterior curotomy and fracture by medial displacement with a pick.

The mucosa over the promontory and the horizontal portion of the facial nerve anteriorly are removed. Gelfoam soaked in 1:1000 solution of epinephrine is placed over the stapes footplate. The vein graft is freed of its fat and areolar tissue and is divided; it is

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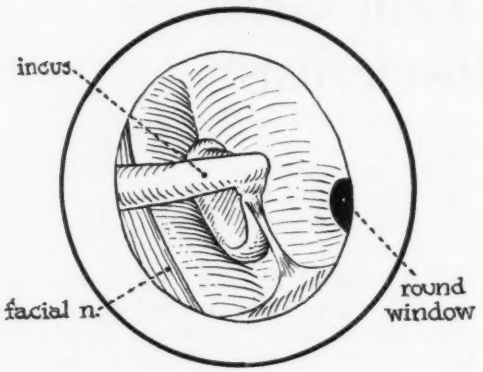
†From the Department of Otolaryngology, Louisiana State University School of Medicine, New Orleans, La.

FIG. 1



Adequate removal of external aditus gives good exposure of middle ear and its pathology.

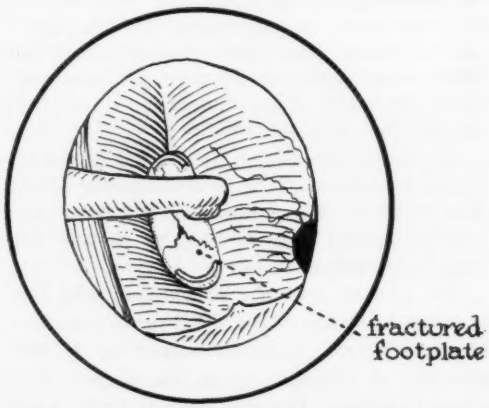
placed on the promontory with the intima side up.

The Gelfoam is then removed from the footplate area which shows a dry bloodless field. This is essential before working on the footplate. The footplate if thin may be fractured in the center (Fig. 2). The fragments are removed with fine picks until the fossa ovalis is of normal size and shape (Fig. 3). In many cases the footplate shows thick otosclerosis and requires removal with a Shea cutting burr.

The vein graft is then placed in position over the new fenestra with the intima up and adventitial side down.

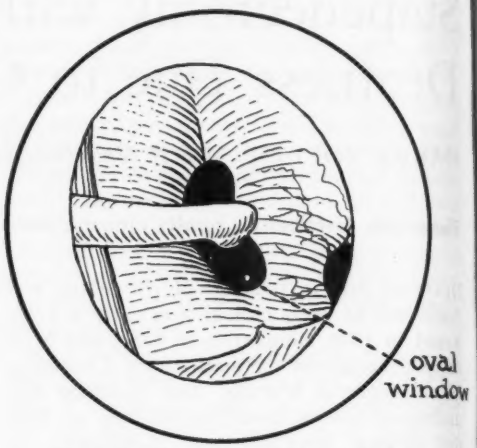
A polyethylene plastic strut of proper length

FIG. 2



The stapedius tendon has been divided, the stapes fractured and removed. The thin footplate is fragmented.

FIG. 3

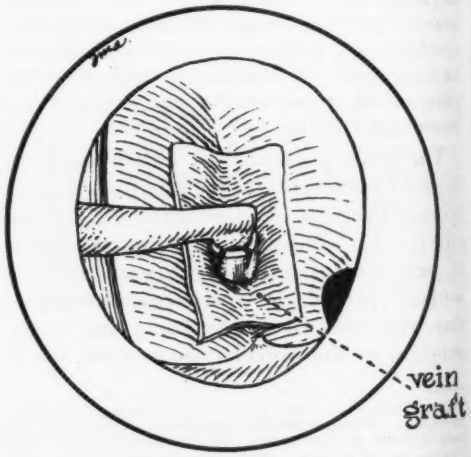


The oval window after removal of the footplate.

is cut to fit between the lenticular process of the incus and the oval window. A small grasping forceps positions the tube with the beveled end invaginating the graft partially into the oval window. The collar is fitted snugly into the lenticular process of the incus. The vein is then pulled taut so it is free of wrinkles (Fig. 4).

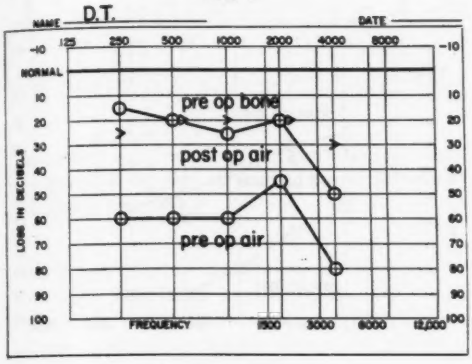
The eardrum is then replaced and Gelfoam saturated with 1:1000 solution of epinephrine is placed over the incision. The ear is lightly packed with a large piece of cotton lubricated with an antibiotic ointment. The patient now

FIG. 4



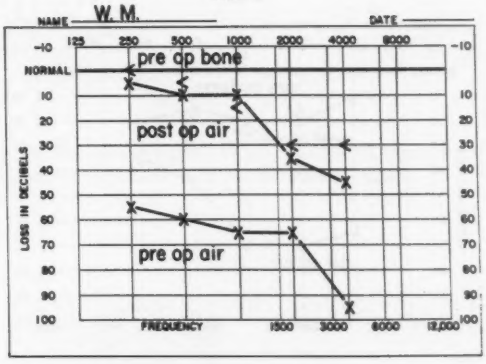
The vein graft and polyethylene strut in position.

FIG. 5



Closure air-bone gap.

FIG. 7



Closure air-bone gap.

hears better and the Rinne test will be positive.

Upon returning to his room the patient is instructed to lie on the ear which was not operated upon and to restrict head movements. This will lessen a vestibular reaction. The patient is given antibiotics, an antihistamine, and dimenhydrinate (Dramamine). The period of hospitalization is usually two days. During the convalescent period at home the patient is maintained on the above drugs for a week.

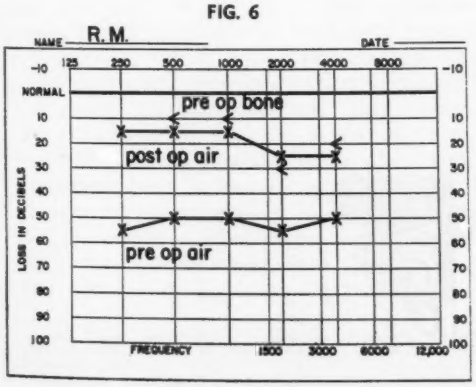
Results

Air-bone gap closures for the 500, 1,000, and 2,000 cycles per second constitutes a good measure of success (Figs. 5-11). This closure represents a difference of 10 decibels between the preoperative bone and the postoperative air conduction in the speech frequencies. In this series approximately 80% had a positive air-bone closure, 95% gained at least 15 decibels, 90% exceeded the 30 decibel level, and 25% reached the 15 decibel level or better. Three patients showed no significant improvement. However, in 2 cases a second operation attained a closure of the air-bone gap. The failure in the first case was due to displacement of the stent and in the second enlargment of the fossa ovalis was required. The other patient will be explored at a later date. Stapedectomy is an excellent procedure for the rehabilitation of deafness due to otosclerosis with stapes fixation. In time a great deal of information will be obtained as to the tolerance of the vein graft and the plastic stent as well as the lasting improvement of hearing.

Summary

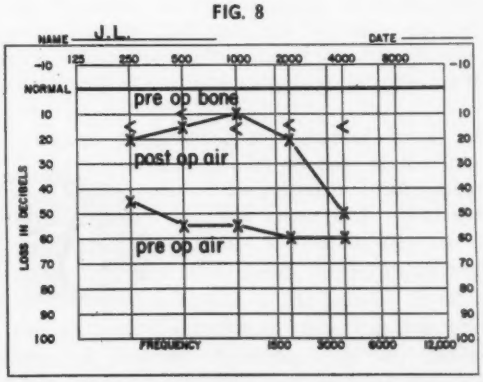
Deafness due to stapes fixation was discovered as early as 1735. Improvement of hearing was accomplished by mobilization of the stapes. The procedure was discontinued

FIG. 6



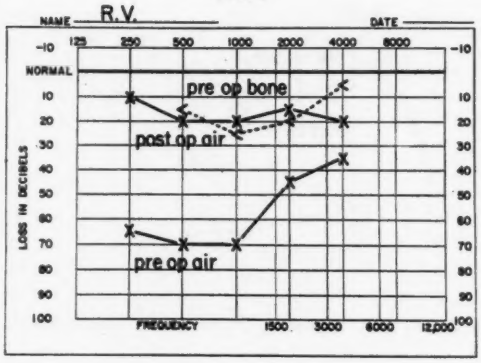
Closure of air-bone gap.

FIG. 8



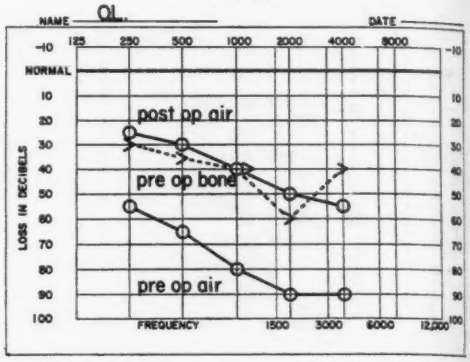
Closure of air-bone gap with 15 decibel speech range.

FIG. 9



Overclosure of the air-bone gap.

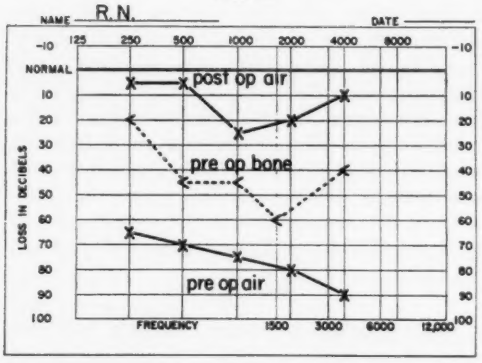
FIG. 11



Overclosure of air-bone gap. Repeat audiogram showed marked overclosure.

in 1899 and re-introduced by Rosen in 1952. Portmann and Shea described fenestration of the oval window and covering the fossa ovalis with a vein graft. Ossicular continuity is re-established with the stapes or a plastic polyethylene strut. Results showed a positive air-bone closure in 80% of the cases, a gain of 15 decibels or more in 95 per cent. Hearing exceeding the 30 decibel threshold level occurred in 90% of the patients. Stapedectomy has given better hearing results than previous methods for the rehabilitation of the otosclerotic with stapes fixation. In time we will have further information as to the long-term hearing improvement.

FIG. 10



Marked overclosure of the air-bone gap.

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Thrombolytic Therapy*

SOL SHERRY, M.D.,† *St. Louis, Mo.*

The use of enzymes for the dissolution of clots is still in the investigative stage. Yet such agents are available on the market. The doctor who would use these substances will do well to read this paper carefully.

THE TREATMENT of thrombo-embolic disorders with clot dissolving agents represents an exciting and new therapeutic approach to a serious medical problem. Considerable progress has been made in this development and it will be my purpose to indicate the current status of this endeavor.

It has been demonstrated in a number of laboratories that clots, produced experimentally in the arteries and veins of animals, can be dissolved by the use of appropriate enzymatic agents. On the left in figure 1 is shown a biopsy of the femoral artery of a dog taken on the fifth day after the experimental production of a thrombus. In this control animal the artery can be seen to be occluded completely by a thrombus undergoing early organization. On your right is shown a biopsy taken from an animal in which a similar thrombus had been induced but was subsequently treated with a fibrinolytic agent. The clot is almost completely dissolved with only small fragments of the original thrombus remaining.

FIG. 1

Similar studies have now been extended to man where, again, it can be shown that thrombi can be lysed by enzymatic means. Figure 2, taken from the work of Johnson and McCarty,[1] shows on the left, a normal venogram in a peripheral vein of a human volunteer. A course dental broach then was inserted through the venipuncture needle and the intima of the vein wall traumatized. Twenty-four hours later the venogram in the center reveals the presence of an obstructing thrombus which, by palpation, extended for a distance of approximately 15 cm. Following this procedure, a fibrinolytic agent was administered intravenously into the opposite arm over a 24 hour period. After the completion of the treatment, the venogram on the right reveals the complete restoration of blood flow.

Recently the problem of developing a practical and effective form of thrombolytic therapy has become complicated by the introduction of pharmaceutical preparations. Thus, we are concerned not only with the further development of thrombolytic therapy, but must soberly and critically appraise the accomplishments made possible by the pharmaceutical preparations currently available for use.

Before considering the current status of thrombolytic therapy, let us first discuss certain basic aspects of the problem. In thrombolytic therapy, we are concerned with the enzymatic dissolution of the fibrin in a thrombus, and this must be accomplished without undue hazard to the patient. From a pharmacologic standpoint then, our immediate and primary objective, with any fibrinolytic agent, is to raise and regulate the clot

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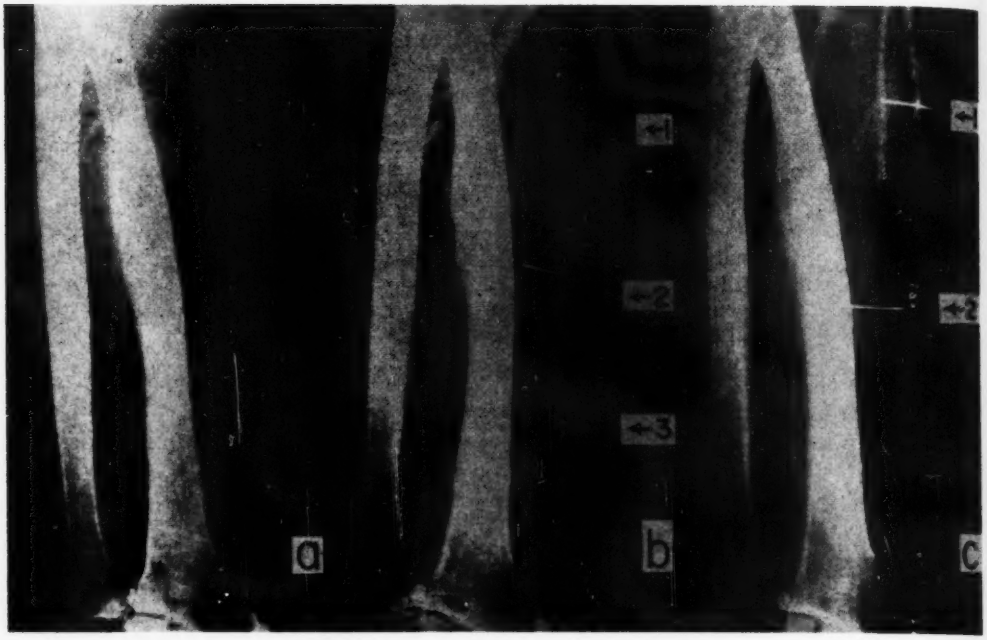
†From the Department of Internal Medicine, Washington University School of Medicine, St. Louis, Mo.

FIG. 2



Reprinted with the permission of Johnson and McCarty.[1]

dissolving or thrombolytic activity of the circulating plasma. To understand the real meaning of an increased ability of the plasma to dissolve clots, we must first consider how clots are normally dissolved.

As is shown in figure 3, clots are uniquely adapted to undergo dissolution, for they contain within their interstices a naturally occurring fibrinolytic enzyme system which is normally present in an inactive form termed plasminogen or profibrinolysin. In the presence of an activator or kinase, a specific type of enzyme itself, the plasminogen is converted to plasmin, a proteolytic enzyme capable of dissolving fibrin.

Plasmin is very similar to trypsin in its action. It can digest a great variety of proteins, but *inside the clot* plasmin only has fibrin available for digestion and there is little to inhibit the breakdown of this fibrous protein. Thus, the body needs only to bring an activator to the clot to effect its dissolution. Indeed, extensive studies have revealed that the body uses just such a mechanism in effecting the natural resolution of fibrin and thrombi. Following appropriate stimulation such as intense exercise, ischemia, or after the administration of epinephrine, the body responds by releasing an activator into the circulation and this results in an enhanced clot dissolving activity of the plasma.

Since the ability of the plasma to dissolve clots is directly related to content of its activator, a logical approach to thrombolytic therapy is to control the activator level of the plasma. As is shown in the upper portion of figure 4, plasminogen activators induce a thrombolytic action whether these activators are present in a purified system or in plasma.

Two approaches are currently available to us: either to control directly the activator

FIG. 3

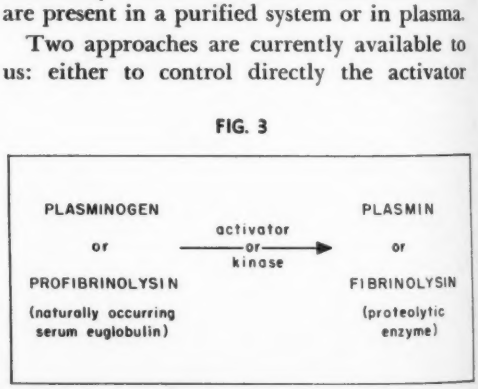
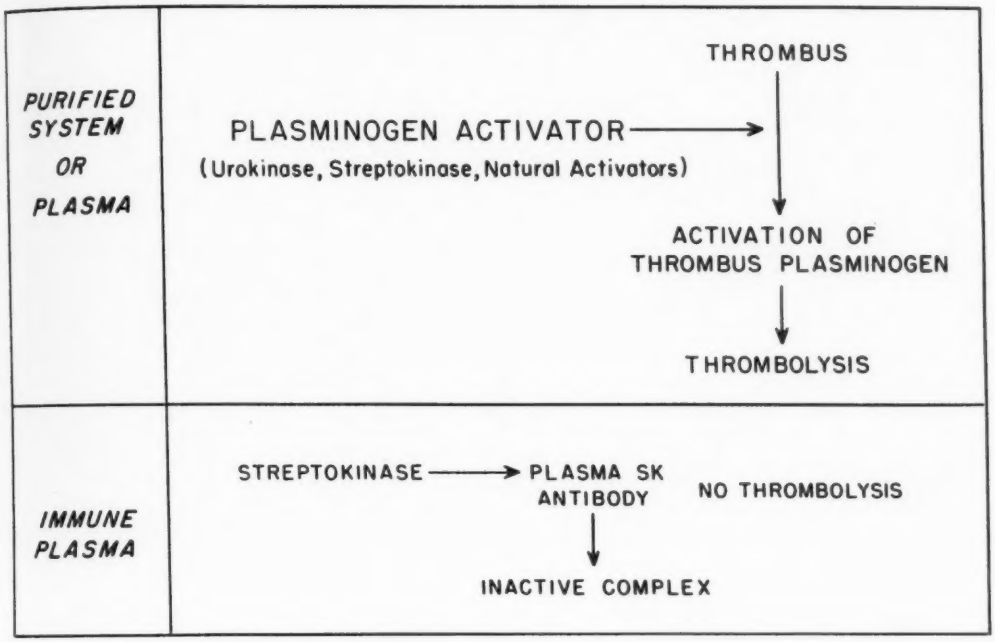


FIG. 4

SIMILAR EFFECTS OF PLASMINOGEN ACTIVATOR IN VIVO AND IN VITRO



level by the infusion of purified activators, as for example, by using the bacterial activator streptokinase, or by infusing urokinase, the activator found in human urine. On the other hand it is also possible that we might control the endogenous release of the naturally occurring tissue activators.

At present it is not yet feasible to control satisfactorily the release of the natural activator by pharmacologic means though such an approach would be most desirable. Some investigators have explored the use of purified bacterial pyrogens for this purpose, and others have investigated nicotinic acid and its derivatives. Though these substances cause a release of endogenous activator, they are inconsistent in producing this effect and tolerance to the agent develops very rapidly.

More direct control of the levels of activator can be achieved, at present, by the direct infusion of activator preparations. Though human urokinase, the urinary activator, would have distinct advantages because of its presumed nonantigenicity, it is not available in sufficient purity for investigational studies in man. Considerable progress in the purification of urokinase already has been made; further developments may make this agent available in the near future.

However, it is possible at present to control the level of circulating activator by the infusion of highly purified streptokinase. As is shown in the lower half of figure 4, special immunologic considerations arise when streptokinase, which is derived from hemolytic streptococci, is used for therapeutic purposes. Since streptococcal infections are a relatively common event, human plasma contains a variable concentration of specific streptokinase antibody which immediately renders streptokinase inert. As a consequence, the induction of a thrombolytic state with streptokinase requires the administration of sufficient agent to exceed the previously acquired resistance of the plasma to this agent; this resistance may vary as much as a thousandfold among patients. Thus, when streptokinase is used the dose must be individualized for each patient, and the amount to be used can only be determined by prior assay of the patient's plasma

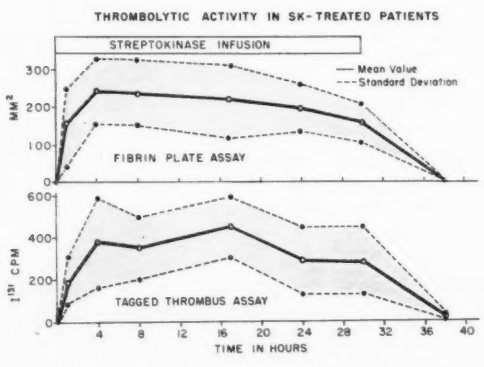
for streptokinase antibody. In no other way can a dose be calculated that will produce a consistent clot dissolving effect in man.

When these considerations are taken into account and an appropriate priming dose given, streptokinase becomes a very useful agent for the induction and control of a regulated thrombolytic state in patients. Figure 5 shows the type of sustained and powerful clot dissolving state induced with streptokinase infusions of 30 hours duration in 40 successive patients suffering from a variety of thrombo-embolic diseases. Displayed are the mean value and standard deviation. The upper section displays plasma thrombolytic activity measured on fibrin plates, and the lower section describes the ability of the patient's plasma to dissolve isotopically labeled preformed human plasma clots. As will be noted, the therapeutic regimen raises the clot dissolving activity of the plasma to 300 to 400 times the normal level and the effect is maintained until the termination of the infusion, when the activity drops off sharply.

It was with streptokinase, used in a manner analagous to that just described, that Johnson and McCarty were able to dissolve experimentally induced blood clots in the veins of human volunteers (Fig. 2).

Another theoretical approach to dissolution of clots in man is by the direct infusion of the enzyme plasmin itself. The upper section of figure 6 displays the simple concept which has been held to justify the use of plasmin infusions in patients. Though plasmin is the enzyme which, when activated in the interstices of the clot, produces rapid dissolution of fibrin, its surface action on preformed clots proceeds at a relatively slow rate. In addition and more importantly, there are grave difficulties concerned with the use of this enzyme when infused into patients. Here we are infusing a proteolytic enzyme much like trypsin, and though plasmin has the ability to digest fibrin, it also is capable of digesting a wide variety of plasma proteins including fibrinogen, accelerator globulin, antihemophilic globulin and some of the components of serum complement. Fortunately, as is shown in the lower section of figure 6, plasma exerts powerful inhibitory effects against plasmin, and where small doses of plasmin are injected, as is currently in vogue, the enzyme is immediately inactivated and no enzymatic effects are produced *in vivo*. Second and of much greater fundamental importance is evidence that the infusion of large doses of plasmin, sufficient to produce detectable clot lysing effects *in vivo*, will cause a state of excessive plasma proteolysis with its attendant hemorrhagic disorder. Many of us have had experience with the catastrophic hemorrhagic consequences of fibrinolysis as a disease state; this disorder is due to hyperplasminemia.

FIG. 5



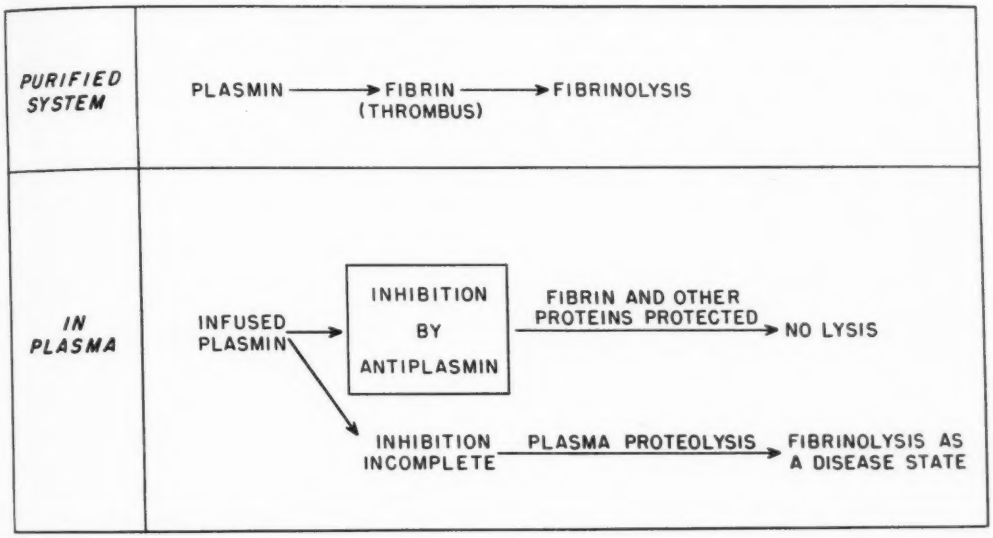
Similar considerations apply to the use of all other conventional proteolytic enzymes so far tested. In all instances low doses of these enzymes, e.g., trypsin, chymotrypsin, etc., are rendered biochemically inactive by plasma inhibitors, and high doses, sufficient to overwhelm plasma inhibitory mechanisms, induce a state of general plasma proteolysis with associated severe coagulation defects.

Now let us turn to a consideration of the thrombolytic agents which have been made available commercially. Actase and Thrombolysin are both designated by their manufacturers as human fibrinolysin or plasmin preparations. On analysis, both preparations are mixtures of streptokinase and plasmin, and it can readily be shown that, upon addition to human plasma, their potential clot dissolving activity resides almost exclusively in their streptokinase content. However, both preparations pose different problems.

Actase contains a small amount of plasmin mixed with a small amount of streptokinase. On analysis, one vial of Actase of 50,000 Ortho fibrinolytic units contains approximately 6,500 units of streptokinase and 5 units of plasmin. One could hardly expect that 1 to 2 vials of such a preparation could

FIG. 6

DISSIMILAR EFFECTS OF PLASMIN IN VIVO AND IN VITRO

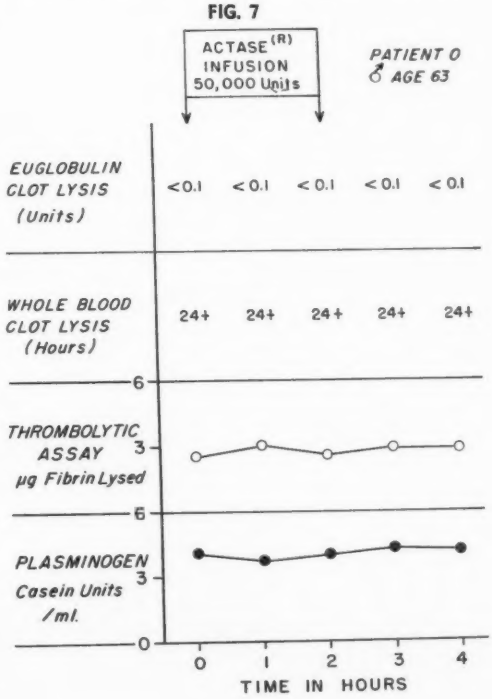

PURIFIED SYSTEM
PLASMIN → FIBRIN (THROMBUS) → FIBRINOLYSIS
IN PLASMA
INFUSED PLASMIN
INHIBITION BY ANTIPLASMIN
FIBRIN AND OTHER PROTEINS PROTECTED → NO LYSIS
INHIBITION INCOMPLETE
PLASMA PROTEOLYSIS → FIBRINOLYSIS AS A DISEASE STATE

raise the clot dissolving activity of the plasma. First, the infusion of 5 to 10 plasmin units over a 2 hour period into a circulating reservoir containing 10,000 to 20,000 inhibitor units cannot be expected to have any effect. Second, the infusion of 6,500 to 13,000 streptokinase units over a similar period into a circulating reservoir containing from 10,000 to 6 million antistreptokinase units, depending on the patient's prior state of immunization, should also prove unrewarding.

The prediction that this agent would fail to raise plasma thrombolytic activity *in vivo* was confirmed by direct experimental trial in man. Shown in figure 7 is the complete lack of effect in one patient but similar observations were made on 5 others. Considering that Actase fails to exert detectable biochemical effects in patients and, in addition, provokes a high incidence of pyrogenic reactions, its clinical use as a clot dissolving agent would appear undesirable.

Thrombolysin, the other preparation currently available, is also a mixture of plasmin and streptokinase. One ampoule of this material, listed as containing 50,000 Merck Sharp & Dohme fibrinolytic units contains approximately 50 plasmin units and 24,000 units of streptokinase. Again the antiplasmin activity of plasma is readily sufficient to inactivate all the plasmin present, and the clot

FIG. 7



dissolving activity of this preparation is also primarily attributable to its streptokinase content. However, there is sufficient streptokinase in this preparation, when used in the dosage of 4 or more ampoules, as recommended by the manufacturer, to induce an active thrombolytic state in some patients. In our own studies with this preparation, it has been possible to reproduce a comparable thrombolytic state in many by infusing streptokinase alone in an amount equivalent to that contained in the mixture. Therefore Thrombolysin should be viewed as a streptokinase preparation containing small amounts of plasmin; its proper use must be governed by the same considerations previously discussed for streptokinase alone, where the dosage for the patient must be individualized depending upon the amount of streptokinase inhibitory material present. The fixed or standard dosage schedule currently recommended by the manufacturer makes it impossible to insure whether the patient will develop an active thrombolytic state or not.

The release of mixtures of streptokinase and plasmin for therapeutic use raises serious problems in standardization. These agents are at present standardized in terms of arbitrary fibrinolytic units and each manufacturer has its own. This requirement for appropriate standardization is emphasized by the finding that both manufacturers list their ampoule as containing 50,000 units yet one preparation contains four times as much streptokinase and 20 times as much plasmin as the other. It would seem wisest, if these agents are to be used properly, that the content of their individual components be known.

Since a satisfactory form of thrombolytic therapy is, in our opinion, not yet available for clinical use, recognition and emphasis must be given to the solution of those problems upon which further progress depends. These include:

First, the choice of agents. From basic considerations it would appear that the emphasis should be on the development of activators, either for direct infusion or by endogenous control of their activity through pharmacologic means.

Currently, streptokinase is the only activator available by which a controlled and regulated thrombolytic state can be induced in the patient. It is not an ideal plasminogen activator for clinical use for its antigenic nature imposes certain restrictions upon and complicates its use. Dosage for the individual patient must be established after prior assay for plasma antibody, and retreatment may prove difficult because of previous immunization. Undoubtedly the greatest need for the future is the development of a nonantigenic plasminogen activator; current work with urokinase offers promise in this direction.

Second, the need for simple laboratory guides for instituting and controlling therapy. It is too much to expect that this type of therapy can be carried out on a hit or miss basis. We still need to develop some simple laboratory tests by which the therapy can be controlled and guided in the patient.

Third, the standardization of agents. Thrombolytic agents should be properly standardized in terms of their components, and simple technics available for estimating dosage. Current standardization is unsatisfactory and relatively little attention has been given to the differing abilities of patients to inhibit these agents.

Fourth, the elimination of pyrogenic contaminants. Thrombolytic agents should not produce such undesirable features as chills, fever and hypotension; such reactions occur with all the preparations in current use or under trial. Since these reactions jeopardize both the therapy and the patient, their cause should be eliminated from the agents or means found for their prevention.

Finally, the need for correlative laboratory and clinical studies. It is evident that enzymatic therapy is not sufficiently developed to encourage its general use under any except clinical investigative circumstances. At our present state of development, limited and carefully designed trials utilizing both clinical and laboratory measurements would yield much more vital developmental information than poorly controlled large scale clinical evaluations. It is my view that the field of thrombolytic therapy, though exciting in promise and scope, is still at the clinical investigational level and should remain so until practical and reasonable, if not complete, solutions are available for all its major problems.

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Some Aspects of the Maternal-Fetal Relationship as Expressed by Circulatory Changes*

A. STARK WOLKOFF, M.D., HERBERT S. HARNED, M.D., and LOREN G. MacKINNEY, M.D.,† *Chapel Hill, N. C.*

Interesting studies have revealed information in regard to the exchange of gases across the placental barrier, between fetal and maternal circulations. However, they seem to play little part in certain complications of pregnancy, such as, for example, postmaturity. Clinically, the condition of the fetal heart during labor provides the index for evaluation of the fetus' state in utero.

In 1955, Professor James Walker of St. Andrews, Scotland, wrote "The Oxygen Environment of the Human Fetus."[1] It was this singular work that stimulated those in the clinically oriented obstetric field toward a study of the blood gases of the maternal-fetal system. The influence on clinicians by Professor Walker and his work was dramatic, and much stimulating research has resulted. Unfortunately, however, several unqualified assumptions have been made when the laboratory data was applied to clinical problems. It was because of these apparent misconceptions that this work was undertaken.

To begin with, an understanding of the physical principles of how the blood gases move from the maternal to the fetal circulation is needed. An expression of the Fick Diffusion Formula has been suggested by Barron[2] (Fig. 1). It is obvious that several variables are at work in such an expression, and so if oxygen, for instance, should move from mother to fetus in greater amounts per unit of time, the numerator must increase in value or the denominator decrease. The physiologic principles are complex and an analysis of these parameters obtuse. Barcroft and Barron[3] were deeply concerned with the principle of concentration gradients and the next slide (Fig. 2) from their monograph illustrates the manner in which hemoglobin takes on oxygen under varying partial pressures of the gas. It is interesting to note that the oxygen gradient between maternal and fetal blood is in the neighborhood of 40 mm. of Hg., whereas that of the human as established by Prystowsky is in the range of 20 mm. of Hg. These data have given veracity to the concept of Grosser and the slope of the gradient curve as related to the various layers and thickness of species different placentas.

Walker[1] sampled cord blood at delivery and correlated the per cent saturation to the gestational age (Fig. 3). He had experimental data showing that the older the gestation was, and especially in the intrapartum period, the lower was the per cent saturation. The practice of inducing postmature pregnancies has been reinforced through his work. If one considers, however, the relationship of the per cent saturation of the fetal blood as seen on the dis-

FIG. 1

$$Q = \frac{(P_m - P_f) \times C_a}{R}$$

$Q \neq$ ml's of oxygen per minute from Maternal to fetal blood.

P_m, P_f $\neq$ the average oxygen pressures in mm. Hg. in the matenal and fetal capillaries respectively.

$C_a \neq$ the surface area of the smaller of the two capillary beds in square mms.

$R \neq$ the resistance offered by the tissues separating the two bloods.

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†From the Departments of Obstetrics, Gynecology, and Pediatrics, University of North Carolina School of Medicine, Chapel Hill, N. C.

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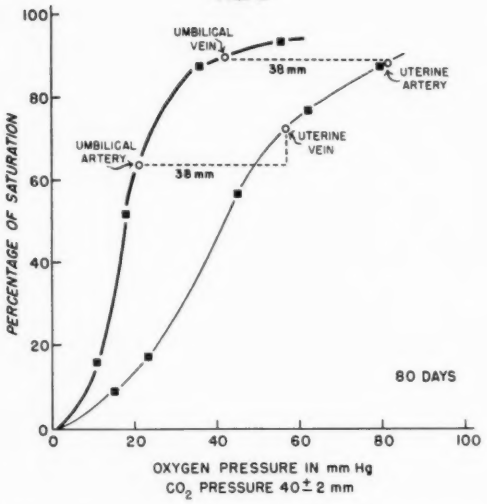
FIG. 2

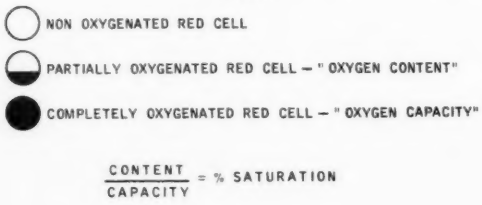


sociation curve, one is struck by the hyperbolic appearance of the curve. Conclusions drawn from per cent saturation of cord blood, without considering the extent the percentage could vary up and down the steep portion of the curve with minimal pressure changes, are certainly suspect. In an attempt to study this interesting phenomenon from yet another viewpoint, and to raise the question on the fallacy of prognosticating the fetal welfare on cord blood samples, the following experiments were carried out. The clinical practice of induction for postmaturity, incidentally, must answer the questions raised by the perinatal mortality figures at the Kings County Hospital between term and postmature pregnancies.[4]

Materials and Methods

Pregnant Shropshire and Dorset hybrids from the Department of Animal Industry, Veterinary Section, of the North Carolina State College, were obtained. These ewes were all approximately at term and weighed from 50 to 60 kilograms sheared. Spinal analgesia was employed exclusively using 10 to 20 mg. of tetracaine. The ewes were then subjected to tracheostomy and intubation and prepared for operation. Paramedian abdominal incisions were made avoiding the large superficial veins.

FIG. 3


NON OXYGENATED RED CELL
PARTIALLY OXYGENATED RED CELL – "OXYGEN CONTENT"
COMPLETELY OXYGENATED RED CELL – "OXYGEN CAPACITY"
CONTENT / CAPACITY = % SATURATION

A Mayo stand was incorporated in the surgical preparations to receive the fetus at the time of hysterotomy. Great care was observed delivering the fetus from the uterus to prevent injury to the cord and its four vessels. Minimum hemorrhage was encountered and the fetus was always delivered as a vertex through the uterine incision which was enlarged with the finger transversely and just sufficient for passage of the muzzle. The head was immediately covered with a saline filled rubber glove to prevent respiration.

The fetus was then strapped on the Mayo stand, and the incisions made for exposure of the femoral veins and arteries and the jugular vein. P. E. 60 polyethylene catheters of known length and caliber were inserted into these vessels and advanced to the right and left sides of the heart itself. The saline and heparin filled catheters were then connected to Touhy adapters and standard 3-way stopcocks. These in turn were attached to nonexpansile fluid-filled tubes leading to P 23 Statham transducers. Recordings were made on a Sanborn Poly-Beam Recording System Model 550M. An Ordway 4-way valve system was used to facilitate the multichannel recording.

The preservation of the integrity and physiologic state of the cord was insured by the use of saline irrigations and 1% lidocaine spray. An indentation in the Mayo stand prevented extraneous pressure on the cord. Without any additional source of heat, the cord was kept intact for hours and with normal fetal vital signs.

General Observations

After spinal anesthesia the ewe's hind quarters collapse. There are no visible signs of altered basal cardiovascular activity. Serial blood pressure determinations taken on ewes subjected to spinal anesthesia with the carotid artery previously exposed surgically has shown no significant alterations in blood pressure.[5]

After the jugular vein has been exposed and catheterized via a 17 gauge needle, the ewe is placed in a dorsal position in an "operating cradle" that permits the limbs to be tied and the head held without pressure. A tracheosto-

my is easily performed in this position. The uterus is exposed, and exploration reveals the presence or absence of twins and locates the fetal head which is held against the uterine wall. The opening of the uterus, exposure of the head in the amniotic sac, and covering the head with a saline filled glove as the membranes are ruptured prevents respiration as described above. After the fetus is placed on the Mayo stand and the cord perfused and protected, it can be immediately detected whether the preparation is healthy by the character of the pulsations and the color of the cord vessels.

The vessels are then cannulated in the prescribed fashion. The position of the catheters can be determined from the oscilloscopic tracings. The aortic and left ventricular tracings are very similar except that the former is slightly more dampened. Apparently the angulation at the aortic arch is too acute to permit the easy passage of the catheter into the ventricle itself.

It has been observed that the right atrial pressure is very closely simulated by an esophageal catheter, and after numerous tracings we are content to observe the esophageal tracing as that of the right atrium. It was an exceptional day when the pulmonary artery was successfully catheterized. Apparently the catheter coils about in the ventricle and only by accident slips through the outflow tract. The cardiac output was performed by using Cardiogreen dye through a Coulson densitometer. The continuous recordings were made over protracted periods, generally several hours. Only one fetus was catheterized at a time; the twin remained in utero, and at the end of the experiment was delivered, usually in good condition, and a second series of recordings taken. Supplementation by oxygen, transfusion or stimulant therapy was not given either the ewe or lamb.

Thirteen ewes and 18 lambs (twins were observed in almost half of the gestations) were used in these experiments. Several of the lambs were taken home for observation. Those in which minimal blood sampling was done survived. These lambs were used subsequently for cinematography purposes in an attempt to visualize the ductus arteriosus.

Results

Figure 4 illustrates a typical recording of the left and right side of the fetal circulation with the umbilical-placental flow intact. The top curve is that of the aorta or left ventricle. The lower curve that of the right ventricle. The calibrations are in mm. of Hg. at the left side of the slide. The average compilations of these recordings are presented in table 1. Frequent sequential fetal blood samples were drawn for blood gas analyses which were done either by the Waters-Conley Oximeter or the Van Slyke method.

An attempt was made next to stimulate the cardiovascular response of the fetus to some noxious stimulus. Either the skin was clamped with a strong hemostat, or the anus was dilated by the same kind of instrument. It can be seen that gasping and respiratory efforts take place and that the left side of the circulation is altered to a minimal extent. Some change is seen in the right heart, however, with a dropped beat and irregular rate as gasping is recorded for a brief moment (Fig. 5).

The most significant result was that seen

FIG. 4

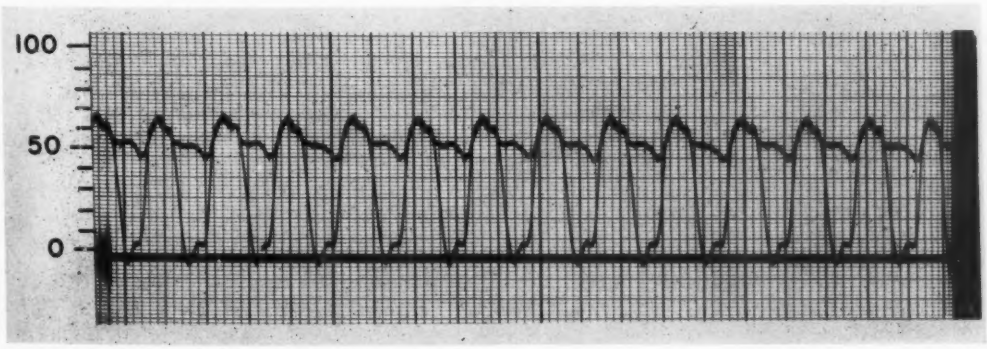


TABLE 1
BASAL DATA

Average pressures	Aorta	64.9/49.8 mm. Hg.
	RV	67/-2.6/4.5 mm. Hg.
	RA	2.0 mm. Hg.
Heart rate	232/min.	
Aorta oxygen saturation	56.8%	
Cardiac output	170 ml./kilo/min.	

when direct pressure was applied to the lamb's head. The magnitude of the pressure exerted has been measured, and the unfavorable response is invariably present at 50 mm. of Hg. and higher. These data agree closely with the uterine forces as determined by Reynolds.[6] As can be seen in figure 6, the initial effect is a slight rise in blood pressure followed by marked arrhythmias and lowering of the blood pressure. It is in this area that the margin of safety, as expressed by such parameters as per cent saturation, oxygen dissociation curves of mother and fetus, the vascular bed of the placenta, and the gas pressure gradients, is exceeded and fetal damage occurs.

Discussion

From an analysis of the tracings and concentrations of the various blood gas components, pH, and other metabolites, the factors that are influential in asphyxia or blood and gas changes in the fetal lamb, are dependent upon profound pathologic alterations in the maternal-fetal system. It has been observed that although the fetus has contributed over 25% of its total blood volume during experimentation for various determinations, there is relatively little change in the pressure of its vascular system, and little if any alteration in the per cent saturation of its blood. The work done on these ewes and their respective lambs has indicated that the fetal heart rate is approximately twice as fast as the human fetal heart. Prolonged tracings have convinced us of the validity of this heart rate, and that from a careful monitoring of this rate certain prognostic implications can be drawn. In the case of a prolonged experiment on one twin, the very fact that the other twin, still in utero, has survived such a traumatic experience as a hysterotomy, prolonged manipulation, and interference to the maternal uterine circulation, gives strength to the thought that the uterine blood flow is a relatively constant feature. At least an adequate amount of exchange is assured even in very abnormal situations as long as the maternal system is maintained. It has been said that in stress conditions the uterine flow could decrease to such an extent that the normal oxygen gradient across the placenta could be lowered. After hours of experimentation we have found the maternal arterial blood to be oxygenated over 80% and little change in fetal oxygen saturation was noted even during

FIG. 5

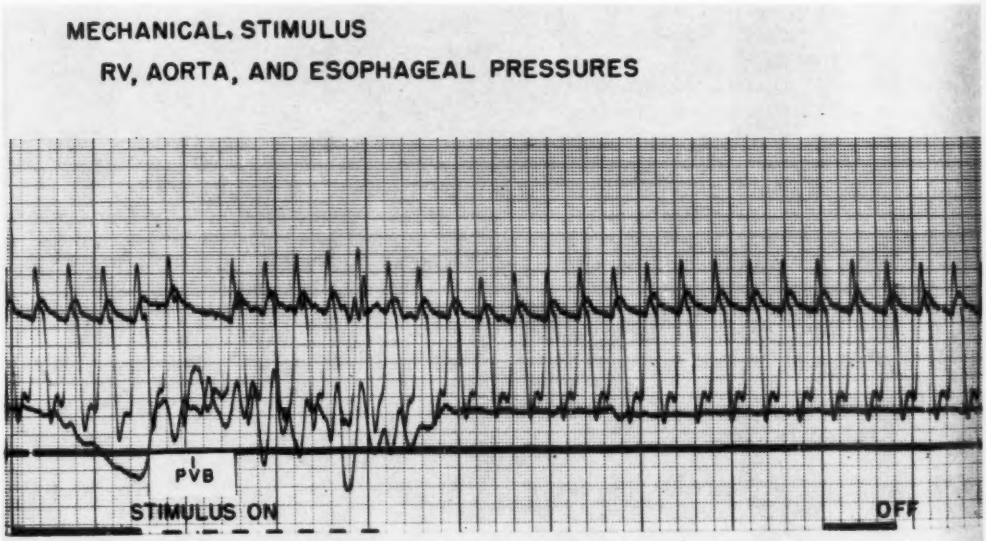
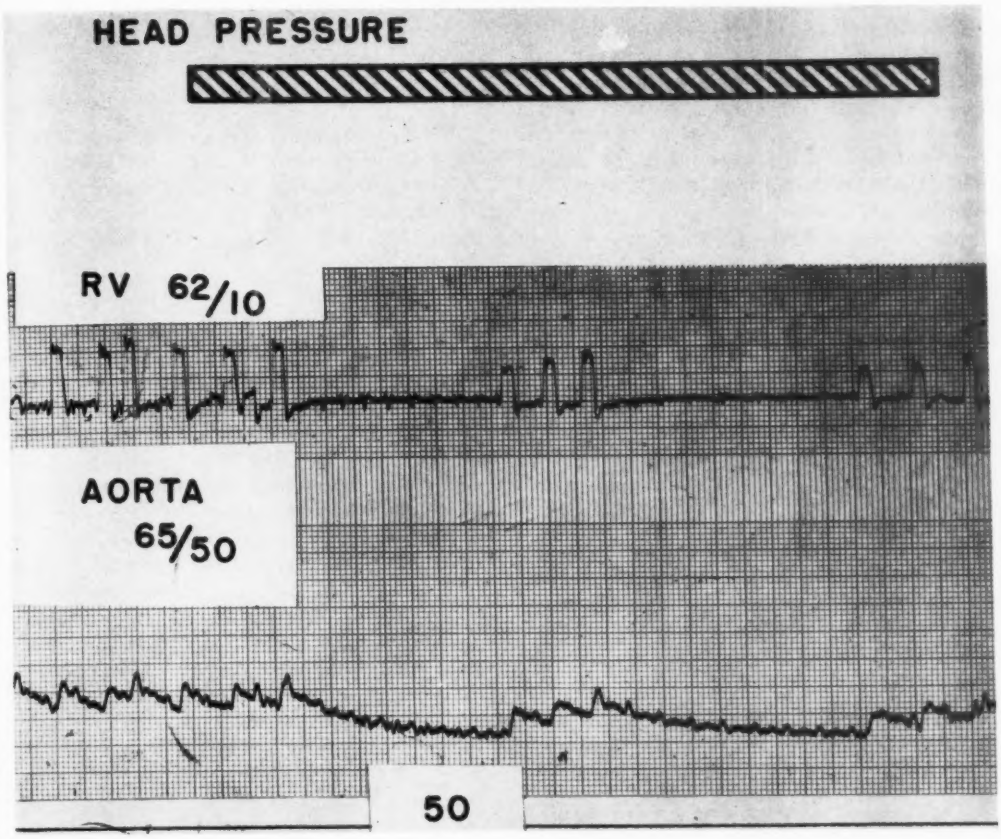


FIG. 6



such critical times. So long as the maternal-fetal circulation was maintained our experimental animal survived; should cord pressure, head pressure, or fetal hemorrhage occur, the tracings showed marked deterioration, the fetus did poorly, and our experiments were foreshortened. It was seen on several occasions that, although the fetal blood oxygen saturation was in the usual range, the fetus was rapidly deteriorating as shown by the slowed fetal heart and irregular rhythm, the per cent saturation being maintained either by longer placental equilibration time, or marked increases in the capillary bed of the placenta.

It is in this area that some disagreement with Walker's work can be found. We have been led to believe that as deterioration sets in from anoxia of prolonged gestation, a rise in the hemoglobin capacity and a lowering of the per cent saturation is observed. Over a long period of time this may well be the case, but for obstetricians busily engaged in problems of the present, the long time deterioration is meaningless. If placental insufficiency can develop in a short period of time, say the length of a labor, we have not been able to reproduce it in our lambs insofar as per cent saturation of the blood or hydrogen ion concentration is concerned, unless maternal-fetal circulation is interferred with. Witness the relatively normal vital signs of the twin still in utero after the uterus has been open for several hours.

The criteria for fetal well-being, then, at least from our experimental data, does not appear to lie in the oxygen concentration either of samples from the cord vessel or placental gradients. It seems that so long as the maternal-fetal blood pressures and circu-

lations are intact and the pumping action of the two hearts vigorous, the blood gases will be exchanged at the rates compatible with intra-uterine life. A study of per cent saturation or gradients of pressure between the two circulations are most important when a consideration of the mechanisms of exchange is sought, but within the scope of the clinical features of pregnancy and childbearing they have little meaning.

The ideas of Gelhorn, Flexner and Hellman[7] on the placental organ as a changing barrier to tagged metabolites, and the profound studies of Plentl and Gray[8] on the origin and fate of amniotic fluid have led many obstetricians to think along the lines of "placental insufficiency." This term is applied to cases in which intrapartum death is seen to occur without obvious etiologic factors discernible. Walker was quite concerned with alterations in per cent saturation with prolonged gestation, and advanced the movement especially in Great Britain of inducing "postmature" mothers. Table 2 gives an analysis of the obstetric experience of Kings County Hospital from 1956-1958. It can be seen that the fetal perinatal mortality associated with postmaturity, i.e. 42 weeks gestational age and over, is of no great significance, and that the real danger existing in pregnancies that have continued longer than 42 weeks lies in the elective induction of labor in these with resulting mechanical obstetric complications.

TABLE 2

KINGS COUNTY HOSPITAL 1951-1956
PER CENT PERINATAL LOSS
BY DURATION OF GESTATION*

Weeks	*Deliveries*	*Fetal Death*		*Neonatal Death*	*Total*
		Prior to Labor	*In Labor*		
38-41	15,040	0.6	0.3	0.4	1.3
42+	3,016	1.0	0.4	0.8	2.3
TOTAL	18,056	0.7	0.3	0.5	1.5
		$p<.00006$			

*Single pregnancies only.

Summary

1. In evaluating the criteria of fetal welfare, the parameters of cord blood saturation, gradient pressure differences between the maternal and fetal circulations, and uterine blood flow have little significance in obstetric management.

2. All of these factors have much to do in establishing mechanisms of placental function and are expressions of compensatory activity in the fetal system.

3. A continuous monitoring of the fetal heart is the best way of evaluating the condition of the fetus in utero.

4. There has been no substantiating experimental evidence to the concept of "placental insufficiency," especially in regard to prolonged gestation.

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CASE REPORT

Insulinoma

ALBERT WEINSTEIN, M.D., and
LOUIS ROSENFELD, M.D.,† *Nashville, Tenn.*,
and HASKELL W. FOX, M.D., *Greeneville, Tenn.*

THE DIAGNOSIS of insulinoma must be made with caution. Patients usually are seen with a history of recurrent confusion, convulsions or coma. They may be directed into psychiatric or neurologic wards, may be labeled epileptic or hysterical, as having cerebral arteriosclerosis, or being suspected of having a brain tumor. The finding of a blood sugar of 50 mg. per 100 ml. or less in the fasting state, or during an attack is highly suggestive of an insulin-producing tumor. The relation of the attack to food intake is important. The seizures occur usually early in the morning before breakfast, or during the day several hours after a meal. They are relieved classically by a feeding of carbohydrate. They may be precipitated by physical or emotional fatigue. This sequence of hypoglycemia, seizures, and relief by glucose, has been styled the triad of Whipple.

The differential diagnosis demands the exclusion of functional hypoglycemia described first by Seale Harris[1] and the alimentary hypoglycemia occurring as part of the post-gastrectomy dumping syndrome. This differentiation is not ordinarily difficult. Nor is there a problem in separating the hypoglycemia associated with widespread hepatic disease, hypopituitarism or Addison's disease. The careful clinician must be aware that hypoglycemia may follow the injection of insulin, self-administered by a nondiabetic patient for reasons of his own choosing. Difficulty at times may be encountered in the differentiation of the hypoglycemia associated with hypothalamic lesions following encephalitis.

Another cause of hypoglycemia that is difficult to diagnose is that secondary to disease of the pancreas and adjacent organs which has resulted in neoformation of pancreatic insular tissue.[2] In these cases this insular tissue is composed chiefly of beta cells. Consequently, although insulin is produced, since alpha cells are absent, glucagon is not available and a relative hyperinsulinism results.

From the standpoint of diagnosis of an insulinoma, the single most important procedure is the finding of a fasting blood sugar of 50 mg. per 100 ml. or lower. Sometimes a 36 to 48 hour fast, or even added physical exercise, may be necessary to create this diagnostic degree of hypoglycemia. This simple procedure is more reliable than the glucose tolerance test. We have not used tolbutamide intravenously and believe it might even be a hazardous procedure.

A recent publication by Trajans and his collaborators[10] reports the use of tolbutamide intravenously in the differential diagnosis of the hypoglycemic state. They indicate its value in patients suspected of having an insulinoma, who present normal or borderline fasting blood sugar levels. In those patients who have fasting hypoglycemia "it (intra-venous tolbutamide) should be given with great caution."

Recently we have cared for an elderly lady who had suffered for 8 years with episodes of fainting. The diagnosis of an islet cell tumor of the pancreas was made. The tumor was resected successfully and the patient has been cured.

In looking into the records of the Vanderbilt University Hospital, we were interested in learning that this diagnosis has been verified at operation or autopsy in only 7 patients since 1925.

In 1958, a 54 year old white man was admitted to Central State Hospital for the in-

†From the Departments of Medicine and Surgery, Vanderbilt University School of Medicine, Nashville, Tenn.

sane, because of convulsions. He was seen there by Dr. Rudolph Kampmeier, who suspected an insulinoma. Fasting blood sugar levels were extremely low, 37 to 42 mg. per 100 ml. Operation revealed a small adenoma in the body of the pancreas. A wedge resection was carried out, but this was followed by the development of a pseudocyst, staphylococcal septicemia and death.

In 1956, a 33 year old white woman had drowsy attacks and fainting spells. Fasting blood sugar levels were at 40 mg. per 100 ml. At operation no pancreatic or aberrant tumors were found. The body and tail of the pancreas were resected empirically. The patient continued to be symptomatic and to have hypoglycemia. She has been benefited by cortisone, orally, subsequent to the operation.

In 1940, a 51 year old white woman had spells associated with blood sugar levels of 24 and 30 mg. per 100 ml. Surgical exploration did not reveal a pancreatic tumor, and none of the pancreas was resected. Follow-up information is not available.

In 4 other patients who died from either cardiac or malignant disease and who came to autopsy, a microscopic adenoma was found. These had no relationship to the cause of death and had not been producing symptoms.

During this 35 year period, 294,454 patients were studied on the wards and in the dispensary of Vanderbilt University Hospital. In addition, 7,118 autopsies have been done. There is no ready explanation for the infrequency of this tumor in this area. On the other hand, in the 30 years, 1929-1959, at the Toronto General and Sunnybrook Hospitals in Montreal, 22 patients were operated on for islet cell adenomas.[3] Seventeen were benign, 5 malignant. Sixteen of the benign tumors were functioning, producing hyperinsulinism. Two of the 5 malignant tumors were associated with metastases, and one was causing hypoglycemia. One patient had a return of hypoglycemia, and 7 years after the first operation was explored again, and another adenoma found. It is of interest that 14 of the 22 patients were women, and 14 of the 22 were 30 to 50 years of age. The 17 benign tumors were distributed rather evenly in the pancreas, 5 in the head, 6 in the body, and 6 in the tail.

Inasmuch as insulinomas may be multiple, or even ectopic, careful surgical exploration is essential in each instance. In describing the surgical management, Williams and Ellison[4] indicated if a single nodule was found in the head of the pancreas, it was enucleated; if multiple tumors were found, pancreaticduodenectomy was carried out. As a surgical complication pseudocysts may form, with fistula which may remain for a long time.

The first correct preoperative diagnosis of a functioning islet cell tumor was made in 1927, by Wilder,[5] at the Mayo Clinic. This diagnosis was confirmed at operation by W. J. Mayo, and a malignant adenoma found. This tumor proved to be fatal. In 1929, Graham did the first successful removal of a hyperfunctioning insulinoma and the patient was cured.[6] Since then many patients have been operated upon and cured.

We wish to report a classical example of a hyperfunctioning insulinoma with successful surgical cure. This is the first such instance at the Vanderbilt University Hospital.

L. L. M. (No. 308,109): The patient, a 68 year old white woman, was referred by Dr. Haskell Fox of Greenville, Tenn., and was admitted to Vanderbilt University Hospital on June 18, 1960. Dr. Fox had made the observation of recurrent hypoglycemia and suggested the diagnosis of insulinoma. He had found a fasting blood sugar of 42 mg. per 100 ml.

For 8 years the patient had had recurrent episodes of nervousness and unconsciousness. The attacks usually occurred just before the evening meal and were relieved by food. At times she was found wandering in a confused state in unusual areas of her home town, even though she had been apparently normal and alert when she departed from home. She would be helped home where those who were awere of her problem would give her food and consciousness would return. The patient had tried to prevent attacks by the frequent eating of sweets, particularly honey, but had not been completely successful. There had been no convulsions; no unusual sweating or hunger. Her health prior to 8 years ago had been excellent. There were no urinary symptoms.

Physical examination: Her height was 66 inches, weight 148 pounds, T. 98.6° F., and B.P. 140/94 mm. Hg.

She did not appear ill; nutrition was normal. The fundi showed no unusual degree of arteriosclerosis. The thyroid was normal, and the carotid sinus was not unduly sensitive. Heart and lungs were normal. The abdomen was markedly distended in the lower half. The tumor was smooth, moderately firm, and extended from flank to flank. No free fluid was present and no evidence of superficial collateral circulation was evident on the abdominal wall. By pelvic examination the pelvic viscera were normal and not associated with the abdominal tumor. Reflexes were normal.

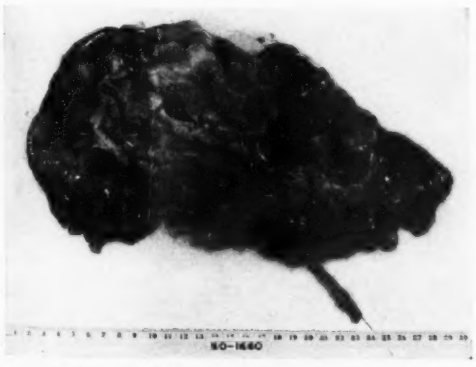
Laboratory data: Urine showed a pH of 7; specific gravity 1.028, 4 to 5 WBC. per hpf. with no RBC. or casts. Hgb. was 15.7 Gm., PCV. 49%; WBC. count 6,550 with a normal differential picture, and E.S.R. of 25 mm. Fasting blood sugar (Folin-Wu) was 36 mg., N.P.N. 38 mg., total serum proteins 6.7 Gm., with an A/G ratio of 3.6/3.1, serum calcium 8 mg., phosphorous 3 mg., bilirubin 0.1 mg. direct, 0.3 mg. indirect, and cholesterol 220 mg. per 100 ml. Determinations also showed a serum amylase of 382 (Somogyi units); a cephalin flocculation of 3+, thymol turbidity of 9 units and alkaline phosphatase of 3.1 (Bodansky units). The VDRL. was nonreactive. Lumbar puncture revealed clear fluid, with pressure and dynamics normal, a protein of 31 mg. per 100 ml., and no cells. Glucose tolerance test showed, fasting 36, (100 Gm. of glucose by mouth), 30 min. 86, 1 hr. 119, 2 hrs. 154, 3 hrs. 104, 4 hrs. 76, 5 hrs. 37, and 6 hrs. 43 mg. per 100 ml. X-ray examinations: Chest was negative. Intravenous pyelogram demonstrated a normal pelvis in the left kidney. There was a suggestion that some dye was appearing in a large right hydronephrotic kidney. Calcification in this area was also noted. EKG. was normal. EEG. showed evidence of some generalized cortical dysfunction.

It seemed the patient had two problems, a hydronephrotic kidney and an insulinoma, but it appeared possible that a single tumor might be present, such as a teratoma containing pancreatic tissue, or an insulin-producing mesodermal fibrogenic sarcoma.[7]

The patient was prepared for operation by the injection of 120 units of corticotropin-zinc in divided doses the day before operation.

At operation on June 24 (by L. R.), upon opening the abdomen a large hydronephrotic right kidney, the size of a football, presented itself and was removed. It was found to contain stones. Because the patient's condition seemed good, exploration of the upper abdomen was carried out, and a nodule 1 by 1.5 cm. was found in the mid-body of the pancreas. It was closely adjacent to the pancreatic duct and accordingly the pancreas was divided at the level of the portal vein, and the body and tail of the pancreas and spleen were removed. Five hundred cc. of whole blood was given during the procedure. (The tumor was not removed by means of a wedge resection for fear of the subsequent development of a pancreatic fistula.)

FIG. 1



Hydronephrotic kidney (collapsed, after removal).

FIG. 2

Benign functioning insulinoma.

The patient had no postoperative difficulties. Intravenous fluids containing glucose were given for the next 4 days; then a routine liquid diet started. Corticotropin was given daily, and then gradually was reduced and discontinued on the 4th postoperative day. The patient was discharged on the 11th postoperative day. Fasting blood sugar determinations varied from 86 to 199 mg. thereafter.

Histologic study indicated a greatly hydronephrotic kidney with secondary atrophy (Fig. 1). The spleen was normal. The pancreatic tissue measured 10 cm. in length; 1.5 cm. from the divided margin was a 1 cm. well-circumscribed, firm, grey-white tumor. Microscopically this was a benign functional nesidioblastoma or insulinoma. The remainder of the pancreatic tissue was normal (Fig. 2). There were nests of epithelial islet cells which appeared to be normal.

Comment. A 68 year old woman who had had fainting spells for several years was demonstrated to have recurrent hypoglycemia. At operation an insulinoma situated in the body of the pancreas was removed, during a subtotal pancreatectomy. Before the pancreatectomy could be done, a football-sized right hydronephrotic kidney was removed; during the course of the pancreatectomy a splenectomy was necessary. The patient has remained well since operation.

On Feb. 7, 1961, the patient was found to be in an excellent state of nutrition. She had no further episodes of unconsciousness. The oral glucose tolerance test was repeated, and now shows no tendency toward hypoglycemia (Table 1). The intravenous tolbutamide test indicates that the patient probably has no more than the normal number of responsive pancreatic islet beta cells, although

TABLE 1

ORAL GLUCOSE TOLERANCE TESTS—BEFORE AND AFTER REMOVAL OF INSULINOMA (March 24, 1960)

	March 20, 1960	*Feb. 7, 1961*
Fasting	36*	96*
100 Gm. glucose orally		
30 min.	86	114
1 hr.	119	111
2 hrs.	154	90
3 hrs.	104	93
4 hrs.	76	108
5 hrs.	37	111
6 hrs.	43	

*Venous blood sugars—mg. per 100 ml. (Folin-Wu).

the test was terminated at 40 minutes (Table 2).

In 1950, Howard and his collaborators[8] reviewed the published literature relative to islet cell tumors of the pancreas. A total of 398 cases were collected; 78.6% were benign, and 12% were malignant. The tumors were occasionally multiple and in some were situated outside of the pancreas itself. More than 73% of the tumors were situated in the tail and body of the pancreas. The patients were between 35 and 60 years of age. More than 80% of the patients were cured. Four had a recurrence of symptoms and were explored again. Essentially all of the patients had temporary hyperglycemia and glycosuria postoperatively, and 4 patients were made diabetic permanently. When a tumor could not be found, the empiric removal of the tail and body of the pancreas was curative in about 50% of the patients. There was an over-all operative mortality of 7 per cent.

In 1949, Crain and Thorn[9] analyzed the 258 cases of insulinoma reported to Jan. 1, 1949. About 11% (29 cases) were associated with other endocrine disturbances. An awareness of possible abnormalities of the adrenal cortex is important from the standpoint of postoperative complications.

TABLE 2

INTRAVENOUS TOLBUTAMIDE TEST (Feb. 11, 1961)

Fasting	92*
1 Gm. tolbutamide (I.V.)	
10 min.	77
20 min.	62
30 min.	62
40 min.	62

*Venous blood sugar—mg. per 100 ml. (Folin-Wu).

The literature was reviewed for the years 1950-1960 and during these years an additional 112 cases were reported. Accordingly, since the first islet tumor was described in 1927, about 510 cases have been reported.

Summary

Hypoglycemia may occur as a consequence of abnormalities in intestinal absorption or as a result of inflammatory disease of the pancreas or the brain. It may be seen in patients with hepatic disease or with abnormalities due to tumor, destruction or inflammations of many of the various members of the endocrine system. Finally, it may be the result of an over-production of insulin in the presence of an islet cell tumor. The symptomatology may be varied and bizarre. These patients are often misdiagnosed and may be judged to have functional disorders or organic brain disease.

Although an insulinoma will be discovered infrequently, the occasional correct diagnosis and successful surgical treatment is a rewarding experience. Alloxan has not proved practical as an agent to specifically destroy the beta cells in the islet. The treatment is surgical and is usually difficult. The tumors are malignant in more than 10% of the cases.

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The Role of Antimicrobial Agents in the Care of the Pediatric Surgical Patient*

HARVEY R. BERNARD, M.D., and
WILLIAM R. COLE, M.D.,† *St. Louis, Mo.*

The authors give critical consideration to the indications for and the contraindications against the routine use of antibiotics prophylactically in pediatric (and for that matter in any form) surgery.

THE EFFECTIVENESS of the antimicrobial drugs has come under increasingly critical scrutiny. This has come about, not only because of mounting scientific curiosity, but because of an increased awareness of complications, either directly or indirectly, referable to the antimicrobial drugs. In addition, the relatively recent series of conflicting reports about the prevalence of surgical and hospital sepsis has focused interest upon objective evaluation of all methods of treating infections.

Most of these reports have dealt with problems primarily referable to the fields of internal medicine and surgery of adults. It is our impression that the knowledge gained from these reports has not been generally applied to the care of the pediatric surgical patient. The question has arisen as to whether pediatric surgical care should follow the same rules that have been established for adults.

While many changes have taken place in the practice of surgery, relatively few improvements have been made in the practice of aseptic technic. On the contrary, the emphasis has been placed upon the development of a great number of chemical and biologic substances devised for the control of microorganisms within the patient, rather than placing more emphasis upon keeping bacteria from gaining entrance to his body. The early successes of antimicrobial therapy for very sensitive organisms, such as the hemolytic streptococcus, the pneumococcus, the gonococcus, and the dysentery bacillus, led to an unfounded hope of preventing all infections with antimicrobials. At one time, nearly every person who was operated upon or suffered an injury, regardless of whether the wound was contaminated or clean, was given some sort of antimicrobial treatment. Later, organisms were found resistant to the first antibiotics discovered and then some organisms that were formerly sensitive to a particular antibiotic became resistant to it. Search for new antimicrobials has gone on relentlessly, hoping that a universal miracle drug might be found. In addition, combinations of antibiotics were concocted hoping thereby to manufacture a "cure all."

During the past decade, there has been increasing evidence that the routine use of antimicrobial drugs after operations and injuries does not prevent postoperative and posttraumatic sepsis, and that in some cases it is actually harmful. In general, the antimicrobial drugs have been found to be most effective when they are used to treat infection produced by microorganisms that have been individually proven to be sensitive to the antimicrobial used. Today the conduct of antimicrobial therapy without ascertainment of the specific antibiotic sensitivities of the organism is remarkably prone to failure. The least effective form of antibiotic use is the giving of broad spectrum bacteriostatic drugs or mixtures of them prophylactically in the hope of preventing infections in persons having diseases of nonbacterial origin. This is really true "shot-gun" therapy, and can only be ineffective unless the shot is the right size for the game hunted.

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†From the Department of Surgery, Washington University School of Medicine and Barnes Hospital, St. Louis, Mo.

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The prophylactic administration of antimicrobial drugs has been effective in the prevention of certain specific infections, questionably effective in the therapy or prevention of less well-defined infections, and perhaps harmful in the prophylactic treatment of still other infections.

In general, antimicrobial prophylaxis has been effective against the beta hemolytic streptococcus, the pneumococcus, the meningococcus, the gonococcus, and the dysentery bacillus (Table 1). Patients with rheumatic fever are protected by antimicrobial prophylaxis against re-infection by the beta hemolytic streptococcus, and against showers of microorganisms during operations, particularly those carried out about the oronasal cavity. A case may be made for the use of continuing and prophylactic antimicrobial therapy for patients suffering pancreatic fibrosis or mucovicidosis,[1] and there are also probably sound reasons for using antimicrobial drugs before and after operations for pulmonary tuberculosis, pulmonary abscesses, etc. A similar case may be made for the use of antimicrobials before and after some operations on the genitourinary tract, during which normal tissue planes are contaminated with antibiotically sensitive organisms.

The advantage of systemic prophylactic antimicrobial therapy and chemotherapy limited to the sterilization of the gastrointestinal tract has been debated. The first suggestion that preoperative antimicrobial sterilization of the gastrointestinal tract might be unnecessary was made by McKittrick and Wheelock,[2] because they found that the routine use of prophylactic antimicrobial therapy, broad spectrum or otherwise, did not reduce the frequency of wound infection or postoperative sepsis. More recently, evidence has been found that the destruction of the normal intestinal bacterial flora by antimicrobials may enhance the local implantability of cancers of the bowel.[3] In addition, there is some evidence that the purging of the normal gastrointestinal flora with antimicrobials may decrease the resistance of animals to systemic infections.[4]

Actually, Weinstein[5] has found that antimicrobial drugs, if not actually harmful, are not beneficial when given to persons having measles either in the eruptive or pre-eruptive phase. So too have the antimicrobial drugs been found to be ineffective in preventing sepsis among patients with inlying urinary catheters,[6] with tracheostomy tubes,[7] or in patients unconscious for long periods of time.[8] The same thing is true of the use of antimicrobial drugs prophylactically during pertussis, mumps, chicken pox, infectious mononucleosis, and poliomyelitis[9] (Table 2). Most of these studies have dealt with the adult medical or surgical patient.

Recently Cole and Bernard[10] have found that prophylactic antimicrobial therapy is of no value to children operated upon for appendicitis (Table 3). In fact, the rate of wound infection following appendectomy among children operated upon before antimicrobial drugs were available was as low as that observed in children operated upon for appendicitis during the last 15 years and given antimicrobial drugs. Surprisingly the rate of wound infections after the removal of the perforated appendix was the same during the pre-antibiotic era as it was during the last 15 years when all children with a perforated appendix received antimicrobial or antibiotic therapy. A questionably significant difference in the mortality rate among the cases of perforative appendicitis, which fa-

TABLE 1

CONDITIONS WHICH WARRANT PROPHYLACTIC ANTIMICROBIALS

Rheumatic fever
Contaminated surgical procedure on patients with diseased heart valves
Mucoviscidosis
Pulmonary resection for tuberculosis
Operation for pulmonary abscess
Operations on the infected genitourinary tract

Table 1 is a list of situations in which there is some evidence that prophylactic antimicrobials are of some value in preventing infectious complications.

TABLE 2

CONDITIONS WHICH DO NOT WARRANT PROPHYLACTIC ANTIMICROBIALS

Measles
Pertussis
Mumps
Chickenpox
Infectious mononucleosis
Poliomyelitis
Inlying urinary catheter
Prolonged unconsciousness
Tracheostomy
Clean surgical procedures

Table 2 lists the situations in which prophylactic antimicrobials have been shown to have no value in preventing infectious complications.

TABLE 3

INFECTION RATE FOLLOWING APPENDECTOMY IN CHILDREN

	Removal of non-perforated appendix 1932-1936 (No antibiotics)	1945-1959 (Antibiotics)
Infection Rate	5.4%	5.3%
	Removal of perforated appendix 1932-1936 (No antibiotics)	1945-1959 (Antibiotics)
Infection Rate	19.0%	23.0%

Table 3 compares the incidence of infection folowing removal of the appendix before antibiotics were available in 1932-1936, with cases that received prophylactic antibiotics from 1945-1959. $P = < 0.5$ in both comparisons.

vored the antimicrobial series, was the only benefit which could be detected in the study of the two series. The indications for chemotherapy in the adult therefore are reasonably well defined. There is good reason to believe that normal children, after the neonatal period passes, may be treated in exactly the same way as adults. Infancy and childhood in themselves do not constitute an indication for prophylactic chemotherapy.

None of the effective antibiotics in use today are without serious side reactions. These reactions include nephrotoxicity, blood dsycrasias, enterocolitis, and allergic reactions of various degrees of severity. In many cases, the observed side-effects are of minor significance and are preventable by careful observation and discontinuance of the drug at the first signs of trouble. However, in a number of instances, when the first signs of bone marrow toxicity, neurotoxicity, or allergic reaction occur, the damage may already be serious, permanent, or even progressive. These reactions, although infrequent, are so serious as to constitute an important consideration in the decision to utilize antimicrobial drugs.

What are the rules for the giving of chemotherapy to children undergoing surgical operation? This problem relates principally to the identity of the organisms involved. Accurate identification of the causative organisms is the first step required toward any effective antimicrobial therapy. Although treatment must at times be started using only an educated guess as to the organism involved, definite steps toward the exact identification of the organism should never be neglected.

The organisms which are associated with surgical infections are of three types: (1) organisms which are always quite sensitive to antimicrobial preparations, such as the pneumococcus, streptococcus, gonococcus, and dysentery bacillus; (2) organisms which are more or less sensitive to antimicrobial therapy, such as the staphylococcus and certain of the gram negative rods; and (3) organisms which are really not sensitive to any antimicrobial drugs, the fungi and viruses.

These organisms may cause surgical infections, or they may cause nonsurgical infections which are associated with surgical operations somewhat by chance.

Nonsurgical Infections

These infections are frequently self-limited, caused by microorganisms which are not responsive to antimicrobial therapy. Measles, pertussis, influenza, and the common cold are examples of this type of infection. Secondary bacterial infection associated with these infections can rarely be prevented by antimicrobial prophylaxis. While drugs capable of treating these infections would be useful, our present drugs are not effective and prophylaxis is neither helpful nor advisable. Fortunately, these infections are usually mild in nature and specific antimicrobial treatment of their complications is effective.

On the other hand, certain specific systemic infections are caused by microorganisms which are very sensitive to available antimicrobial drugs. Examples are tonsillitis, otitis media, meningococcal meningitis, etc. These infections should be treated whenever there is sufficient suspicion of their presence, usually as a consequence of the observation of the cultural characteristics of the causative organism. It is occasionally necessary or advisable as a prophylactic measure to protect other children against these organisms during the rare occurrence of an epidemic. The whole problem of such severe concomitant systemic disease probably is not a great one, for in a review of 961 cases of appendectomy in the St. Louis Children's Hospital over a 20 year period, the incidence of such infections was less than one per cent.[10] No fatalities were noted, and there was almost negligible morbidity.

Surgical Infections

The problem of surgical infection may be divided into two parts, preoperative infections and postoperative infections.

Preoperative infections. This subject is a most complex one. In general it can be said that antimicrobial drugs should be given preoperatively to anyone who has signs of sepsis. They should be given preoperatively therefore to patients having bacterial peritonitis, tuberculosis, pulmonary abscesses, or intra-abdominal abscesses. Insofar as possible, drugs to which the organisms causing the sepsis are sensitive should be used. The giving of antimicrobial drugs before the drainage of well-localized infections unaccompanied by signs of sepsis, and their prolonged use after the drainage or extirpation of the abscess is not warranted, because it is of little value and merely subjects the person to the risk attending the use of the antimicrobials unnecessarily.

Postoperative infections. The use of antimicrobial therapy to treat infections that develop postoperatively depends upon the same basic principles as those determining their use for any infections.

Postoperative infection constitutes the major bacteriologic surgical problem today. It may be divided into three general categories: (1) infections following clean surgical operations, (2) infections following potential contamination of the wound during operation, and (3) infections following contaminated operations.

1. *Infections in clean wounds.* This class of wound is exemplified by herniorraphy, radical mastectomy, and other wounds made under optimal circumstances. Infections do not occur in these wounds unless viable pathogenic organisms are implanted in the wound by virtue of faulty technic (hospital, nursing, or surgical), inadequate sterilization of supplies, or by airborne contamination of the wound. Antimicrobial drugs should not be used in place of asepsis. If the technics are adequate, the drugs are unnecessary and add a needless hazard. As noted by Rousselot,[11] the staphylococci are the organisms usually cultured from these wounds. These organisms are very frequently resistant to the usual antimicrobial drugs. When such an infection occurs, prompt diagnosis and early surgical treatment are usually highly effective.

2. *Potentially contaminated wounds.* Examples of such wounds are those made for operations upon the open gastrointestinal tract, biliary tract, genitourinary tract, and respiratory tract. Few data are available to test objectively the value of antimicrobial prophylaxis for wounds such as these. Over-reliance upon antimicrobial drugs with a tendency toward relaxation of surgical technic may tend to convert all such wounds into truly contaminated ones, whereas scrupulous avoidance of contamination may make such cases more and more like the clean operations. In any potentially contaminated case, if the antimicrobial drugs are to be used, they should be potent, given in therapeutic doses and given for a restricted period of time, i.e., 24 to 48 hours. By these means, exposure of both the organisms and the patient to the drug is effected for a minimal though adequate time for destruction of organisms spilled into the wound during the operation, without camouflaging a latent infection or inducing the growth of resistant organisms in the host. The selection of the drug to be used prophylactically in cases such as this is difficult. The selection must be based upon a knowledge of normal flora in the area invaded and which of the organisms present have pathogenic significance. Cultures should always be taken from wounds such as these before the wound is closed, so that should postoperative infection develop, some knowledge of the organisms likely to be found in it will be had by the time the infection becomes evident.

3. *Contaminated wounds.* Examples are perforative appendicitis, subphrenic abscess, and traumatic wounds from the street, industry, farm and war. Here the prime surgical objective is debridement of dead, dying, or contaminated tissue. The giving of antimicrobial drugs in these cases serves only to reduce the menace of organisms which cannot be removed by the debridement. However, the giving of the antibiotics after debridement of heavily contaminated wounds, such as farm tractor injuries or dirty shrapnel wounds, etc., does not obviate the need for leaving such wounds open for a time, and then practicing their delayed primary or secondary closure. The giving of antimicrobials has not prevented gas gangrene, and other fulminant spreading infections in such wounds. The adage, "When in doubt—leave it open," still applies to the obviously contaminated wound. If it cannot be closed safely

without antibiotics, it very likely cannot be closed safely with them.

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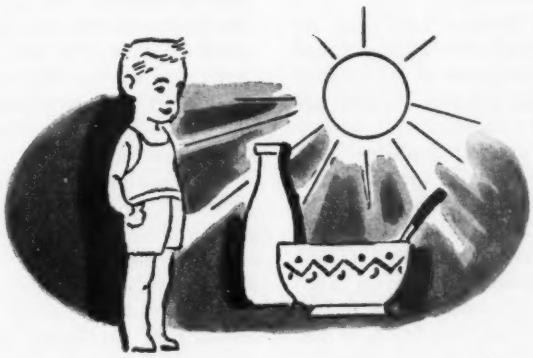


The Role of the Industrial Physician in Compensation Matters As Seen from the Legal Point of View*

THEODORE C. WATERS, *Baltimore, Md.*

The author sets forth the duties of the doctor, as a citizen, to contribute to the implementation of the laws of the States and the Country, whether in industrial cases or in civil litigation.

IN THE ADMINISTRATION of compensation laws two of the most important problems presented to the administrative agency for decision relate to: (1) the fact of injury, and the question as to whether or not it arose out of or in the course of employment; and (2) the evaluation of disability arising therefrom.

These questions are medical and must be decided by the administrative agency upon the medical testimony available in the record. This imposes upon the industrial physician who testifies either pro-claimant or pro-employer and insurer a grave responsibility with respect to the testimony that he offers, either in support of or against the claimant.

Workmen's compensation laws came into being as the result of the social need to remove controversies between employers and employees in the field of common law litigation. They are now effective in all States of the Union. Prior to their enactment, the employer's liability for injuries arising out of and in the course of employment was that imposed by common law, making the employer liable for injuries to the employee caused by the employer's negligence. In other words, a right of action existed in behalf of the employee similar to the present action for damages in traffic accidents. In such litigation, it was incumbent upon the employee to prove negligence on the part of his employer that gave rise to the particular accident complained of. On his part, the employer could interpose the common law defenses on: (1) the employee's assumption of risk; (2) the employee's contributory negligence; or (3) the negligence of the employee's fellow servants.

These defenses were abolished by the enactment of the compensation statutes, making an employer the insurer for the injuries that are compensable under the statutes without regard to the issue of negligence. The preamble and intent of all of the compensation statutes direct the administrative agency to administer and to construe the law liberally in favor of the employee. We are dealing with a type of social legislation to provide prompt, adequate payments to the injured employee immediately after the happening of the accident,—the time when the employee is in greatest need of financial assistance.

We must bear in mind that the enactment of these statutes did two things. First, they made the employer the insurer for the injuries compensable under the statutes. Second, they fixed limits of monetary benefits to employees and deprived them of the right of common law action that previously existed. Therefore, in our approach to the problem that has been assigned to me for discussion, it is important to consider the role that the medical profession could and should play in the administration of these laws.

I believe it is fair to say that today industry has become health conscious; employers realize that the protection of the health of their employees from every type of industrial injury is their legal and moral responsibility. Furthermore, they have readily accepted the responsibility for medical care to their injured employees during the term of their disability. While it is true that in some States full medical benefits are not paid, there are 36 States,*

*Read before the Section on Industrial Medicine and Surgery, Southern Medical Association, Fifty-Fourth Annual Meeting, St. Louis, Mo., Oct. 31-Nov. 3, 1960.

*Alaska, Arizona, Arkansas, California, Connecticut, Delaware, Florida, Hawaii, Idaho, Illinois, Indiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Rhode Island, South Carolina, Texas, Utah, Washington, Wisconsin, Wyoming. United States under the Federal Employers' Act and the Longshoremen's Act.

together with the District of Columbia and Puerto Rico, where full medical benefits are provided for. There are 14 States* with limited benefits. The general trend of legislation has been to increase the payment of medical benefits. Employees on their part are justly demanding the elimination of the potential hazards that exist in industrial exposures with increased benefits in the form of compensation for injuries that may be sustained. Employers on their part realize that the promotion of progress of industrial hygiene and the prevention of injuries have paid dividends in the improvement of industrial relations, the curtailment of compensation costs and increased production, while employees realize that the protection and maintenance of their health is far more important and beneficial than compensation for injuries to their health. It has been my privilege to practice before the compensation commissions in a number of States in the east and while my professional experience has been limited to that section of the country, I have made studies of the compensation laws of the various States. During the time allotted to me it is impossible to present any detailed discussion of the various State compensation laws, but I would like to direct your thought and attention primarily to the need for competent, unbiased, independent medical examiners to either: (1) determine the fact of injury and the question as to whether or not it arose out of and in the course of employment; (2) resolve controverted medical questions that are raised in disputed claims; and (3) advise the administrative agency with respect to the above basic questions.

Since the most important questions involved in compensation cases relate to the medical issues above stated, it is essential that the administrative agency should have the benefit of the best medical opinion that it can receive in order to determine the questions presented to it. Let us consider for just a moment a trial of a compensation case where conflicting medical testimony is offered by the litigants. Many doctors are exceedingly reluctant to testify in Commission or Court proceedings due to interference with their professional engagements, the time consumed in attendance at hearings, and the reluctance to submit to cross-examination. The obvious result is that in many cases the ablest practitioners avoid employment or consultation in cases where they anticipate that the matter will come before a Commission or Court for hearing. While I have the deepest respect for our brothers of the medical profession, the fact is that when a doctor testifies for a claimant, or testifies for an employer and insurer, he naturally has a certain prejudiced point of view with respect to his testimony. In testifying for the claimant, his fee is frequently dependent upon the success of the claim and when a doctor testifies for an employer he feels constrained to review the case in a light as favorable to the employer as is possible. Let's take a simple example. Dr. A may testify on behalf of a claimant that the injured employee has 40% of the loss of the use of a particular member of the body. Dr. B, testifying on behalf of the employer, will testify that the loss of use is ten per cent. Consider the dilemma of the administrative agency in trying to evaluate that testimony. Certainly in this field there is an element of guesswork on the part of the examining physician. Let's admit that he is attempting to give his best opinion but the variance in evaluation of disability always exists. The general policy of administrative agencies and courts has been to interpret the compensation laws liberally and to award what they consider to be adequate compensation for the injuries sustained. In the light of the conflicting testimony how can they decide this question? What better method is available than to have claimant referred to some totally impartial, independent doctor who would resolve the question of disability, advising the administrative agency accordingly. Such a procedure may well avoid excessive medical cost in compensation cases. We all know of the hue and cry that is being raised with respect to these costs. The claimant is not in a position to pay adequate medical costs. The employer is always concerned in keeping costs down.

In my judgment, one of the most important functions of the industrial physician is to familiarize himself with the nature of the process or processes in which the employer-manufacturer is engaged. He should visit the plant, observe these processes and ascertain the potential hazards that may exist with respect to exposure to dusts, fumes, gases, chemical compounds or other elements that may either cause or aggravate disease. If he knows the details of these processes and the various

*Alabama, Colorado, Georgia, Idaho, Kansas, Kentucky, Louisiana, Montana, Pennsylvania, South Dakota, Tennessee, Vermont, Virginia, West Virginia.

items that are used therein, he will be in a much better position to serve the injured employee who is referred to him for examination. Too frequently this phase of the matter is under-emphasized and may result in an improper diagnosis of the injury complained of. Perhaps one of the most important documents in any compensation case is the original report prepared and filed by the examining physician. In my experience these reports have not been sufficiently complete to disclose the real story of the claimant's injury and its relationship to employment. While I recognize the burden that is placed upon doctors who are subject to limitation of time in the preparation of these reports, I honestly believe that this is one of the most important functions that they can serve. A well-prepared report, giving the detail of the incident, the manufacturing process involved, the happening of the accident or the incidence of the disease and their sequelae may often lead to the prompt disposition of the case and avoid trial and litigation that is expensive to all parties. Furthermore, by establishing contact with the company and its employees, the industrial physician assumes a privileged position with the employees; he becomes, in a word, their father-confessor and establishes a medium of confidence in his judgment and actions which prove to be invaluable both to the employees and to the employer. In my judgment there is too little of this in the practice of industrial medicine, and I sincerely believe that if programs of this character were initiated and carried out they would materially assist in the ultimate administration of compensation claims.

With the advent of the amendments to compensation laws making occupational diseases compensable,* the need has been recognized for the appointment of medical boards to resolve the very questions that I am talking about. Time does not permit me any detailed discussion of these laws but I would like to make brief reference to the statutes of the States of Utah and West Virginia, dealing with this subject.

The Utah Code, Annotated, Laws of 1951, Chapter 52, effective May 8, 1951, provides for the appointment of a medical panel with reference to total permanent disability in death cases arising from occupational disease. In controverted cases, the Commission refers the medical aspects of a case to a medical panel appointed by the Commission. That panel examines the claimant, prepares a report in the form prescribed by the Utah law, copies thereof being made available to the parties, and if no objection is filed within a period of 15 days to that report the decision of the panel becomes final. If objection to such report is filed, the matter is set for hearing, at which time the panel members are available for examination and cross-examination, whereupon the Commission renders its final opinion. This is the so-called Utah Plan and from my personal conferences with doctors and counsel who have participated in proceedings under this law it has worked thoroughly successfully since its enactment.

The West Virginia law is contained in Chapter 23, Articles III and IV, as amended, of the official Code of West Virginia. Two boards are established, the first to deal with the disease of silicosis and the second to deal with other occupational diseases incurred in the course of and arising out of employment. To the silicosis medical board is referred all claims for silicosis. As a matter of practice, the claimant is subjected to examination by that board which files such report with the Commission. Thereafter, a hearing is held before the Commission and the parties have the right to introduce such medical evidence that they deem advisable and to examine and cross-examine the doctors who have participated in the examination. At the conclusion of the hearing, the Commission renders its opinion. With respect to other occupational diseases, three licensed physicians are appointed by the Commissioner as a medical board to whom is referred all claims for occupational diseases other than silicosis, with the right of the board to conduct such examinations to determine the fact of injury and the evaluation of disability. The board is also empowered to order an autopsy and the refusal of consent to autopsy operates to bar the claim from compensation. Upon the conclusion of its investigation, the board files its report with the

*Benefits have been extended to compensation for occupational diseases in all States except Mississippi and Wyoming.

Eighteen States provide so-called schedule coverage by specific reference to the disease compensable: Alabama, Arizona, Colorado, Georgia, Idaho, Iowa, Kansas, Louisiana, Maine, Montana, New Hampshire, New Mexico, North Carolina, Oklahoma, South Dakota, Tennessee, Texas, Vermont.

Thirty States provide so-called general coverage which makes compensable any and all occupational diseases: Alaska, Arkansas, California, Connecticut, Delaware, Florida, Hawaii, Illinois, Indiana, Kentucky, Maryland, Massachusetts, Michigan, Minnesota, Missouri, Nebraska, Nevada, New Jersey, New York, North Dakota, Ohio, Oregon, Pennsylvania, Rhode Island, South Carolina, Utah, Virginia, Washington, West Virginia, Wisconsin.

Commission. Copies thereof are distributed to the parties in interest with the right to object to such findings, and have a hearing before the Commissioner, when the members of the board are subject to examination and cross-examination. If no hearing is requested, the report of the majority of the board upon medical questions is conclusive and binding upon the Commissioner, who thereupon passes an order in compliance with the board's decision. If objections are filed a hearing is held, the Commissioner renders his findings in accordance with the testimony that has been presented in the case.

Limitations of time do not permit the discussion of the provisions of other statutes that deal with this important subject, but I am pleased to say that the general trend of legislative action seems to recognize the need for competent, impartial, independent medical advice to the end that justice may be served to parties litigant in proceedings of this type.

While the subject matter of my paper relates to compensation matters, I would like to divert for just a moment to refer to trials of damage cases in courts of law and the role that the physician may play therein. You and I both know of the problem that is presented in jury trial, whether it be on an appeal from a decision in a compensation case or the average run-of-the-mill personal injury case. For your benefit I would like to make brief reference to a rule adopted by the Court of Appeals of my State of Maryland granting authority for the appointment of neutral medical witnesses by trial judges in controverted cases. I quote the following Discovery Rule 5-1 of the General Rules of Practice and Procedure now effective in my State and applicable to all courts therein:

"Whenever the mental or physical condition of a party is material to any matter involved in any proceeding, the court may, upon motion by any party and notice to all other parties, for good cause shown, order such party to submit to a mental or physical examination by a physician or physicians. The order (1) shall specify the time, place, manner, conditions and scope of the examination and the person or persons by whom it is to be made and (2) may regulate the filing of a report of findings and conclusions and the testimony at the trial by the examining physician or physicians, the payment of the expenses of the examination and any other relevant matters."

Commenting on this rule, I quote the following comment in *The Daily Record*, a Baltimore newspaper, under date of Jan. 11, 1955:

"Although the court may not have power in the absence of an application by one of the parties to appoint an expert witness, in most cases where there is wide disagreement between the parties as to the extent of a medical disability, it will probably be found that one of the parties is anxious to have a neutral expert of high standing appointed, and is willing both to make application for such appointment, and to guarantee the payment of the expert's fees. Whether or not to grant the application is in the discretion of the trial judge. The power of the judge to select an expert of his own choice and without the agreement of counsel as to his identity is confirmed by a number of decisions in jurisdictions in which a similar rule is in force."

The question may arise in your minds as to whether or not this rule has been effective. Chief Judge Emory H. Niles of the Supreme Bench of Baltimore City has expressed himself publicly advocating the use of the rule and has applied it in the courts of Baltimore City. However, as a matter of practice we find that in the absence of agreement among the parties to given litigation, the courts will not appoint independent medical experts. This results in the ultimate decision of medical questions being made by 12 men, tried and true, who have no knowledge of the intricate medical testimony that is presented before them. You may well ask as to what, in my opinion, is the answer to this question. My answer is that it can only be corrected by legislative enactment prompted by the education of the general public and their insistence that their duly elected legislative representatives should take affirmative action in what has become an intolerable situation. Perhaps the most significant role to be filled in that connection is to be played by the medical societies such as yours. You have, or should have, the confidence and respect of the various communities in which we live and upon such organizations as yours rests the primary burden in taking the initiative to the end that some solution to this problem may be found.

Perhaps it is not necessary for me to remind the members of this Association of the responsibility of the industrial physician rendering his services in compensation matters. We must bear in mind that in this field of administrative law the injured employees have their first, and in many instances, their only contact with the administration of legal procedure. They deserve and should receive the best possible advice for the determination of medical issues involved in their claims with the burden of high costs for medical testimony. Perhaps it

would be well for the industrial physician in the first instance to try, if possible, to divorce himself from any prejudice pro or con with respect to the claim that he knows is binding, turn a deaf ear to the insistence of counsel who might try to influence his opinion. The public has an interest to serve in the proper administration of these laws and the industrial physician, medical boards and medical examiners may assist materially the administrative agency in the dispatch of its business under these statutes.

Certainly yours is a public service and I believe that if societies such as yours, together with other influential medical associations, will take the initiative in assisting administrative agencies to do the job that the public expects them to do, much of the criticism and fault that is now found with the administration of compensation laws will be abated.

Changing Concepts in Chronic Diseases*

SUMNER YALE ANDELMAN, M.D., *Tulsa, Okla.*

The author reiterates the need for the expansion of facilities for the care of the aged and those chronically ill. The further development of care in the home and in rehabilitation by paramedical professionals is stressed. The medical profession must take the lead otherwise governmental agencies will.

"We wither from our youth, we gasp away sick, sick. . . ." from Byron, *Child Harolde,* is the classical concept of chronic disease today.

The problems of patients suffering from chronic disease or impairment have stimulated new concepts of management by both the medical profession and ancillary medical services. More people are struck each year with chronic disease. Although the lesions of these diseases remain irreversible, it does not mean the outlook is hopeless. Many of the physical, emotional, social and vocational sequelae can be minimized, improved or even eliminated. We can not handle chronically ill patients simply by a prescription blank or by a surgical procedure. We need the combined facilities of the physicians, the community Visiting Nurses Association, the medical-social workers, mobile physical therapy units, and rehabilitation teams who can continue treatment, once begun, right into the patient's home.

The aged or victims of chronic disease may, for practical purposes, be categorized as follows:

(1) The debilitated, infirm, senile, difficult to handle group,—these require tender loving care (T.L.C.) and protection against the turmoils of life, both internal and external. (2) The chronically ill and aged, who through proper medical and rehabilitation services can be restored to a more useful and meaningful life. (3) The major group, composed of those people who have reached an advanced chronologic age but who still live in a biologic age which is imbued with vitality, force and usefulness. They have been shelved by retirement from the vital currents of human endeavor. These people need a new stimulus for their inexhaustible potentials. They need a positive program of activity, not a negative one of limitations. This is a matter that must be of immediate concern to our national leaders. It is beyond the scope of the medical profession alone. I may say that much is being done to consider these people in various fields of endeavor.

Our immediate problem deals mainly with the second group, the so-called "Long-Term Patient." The National Conference of Care of the Long-Term Patient defined such a patient as one who is suffering from chronic disease or impairment, and is likely to need, or has received care, for a continuous period of at least 30 days in a general hospital or continuous care of more than 3 months in another institution or home, such care to include medical supervision and/or assistance in achieving a higher level of self care and independence. This problem includes 30 million people of a population of 180 million people. About 16% of these 30 million are under 35 years of age.

Varying statistics of impairments have been made. The following shows some of the estimates:

(1) About 11 million people suffer from one or another form of rheumatic disease, including the arthritic and the nonarthritic diseases.

(2) Millions suffer from some type of heart disease.

(3) More than two million suffer from "strokes," with or without aphasia.

*Read before the Joint Session on General Practice and Public Health, Southern Medical Association, Fifty-Fourth Annual Meeting, St. Louis, Mo., Oct. 31-Nov. 5, 1960.

(4) About a million have some neurologic disorder, whether cerebral palsy, epilepsy, poliomyelitis, parkinsonism, muscular atrophy or dystrophy, and syphilis of the central nervous system.

(5) Hundreds of thousands have some form of mental disease.

(6) Similar numbers have metabolic diseases, including obesity, diseases of the thyroid and other glands.

(7) Others suffer disability from accidents, whether in the home, industry or by means of transportation.

(8) About 400,000 are blind or have some serious impairment of vision.

We might list other categories with lesser numbers.

Moreover, each year about 20 million Americans, about one out of every nine, enter a hospital for one reason or another. Many of those will become chronically ill.

Despite the dramatic advances in medical technics and the discovery of new miracle drugs, there is an increased incidence of these chronic diseases. This requires an increase in trained professional personnel and facilities for care, including hospitals, rehabilitation centers and services, nursing and convalescent homes, homes for the aged, sheltered work shops and the like. Progress has been made in many fields in research and clinical investigation, but unfortunately there is a time lag between scientific progress and its application at the bedside by the family physician or the nurse. The progress that has been made in the control of pain, palliation for cancer, arthritis, strokes, malnutrition and heart disease, the care of a colostomy and so forth has not been used for the fullest benefit of the patient.

General Principles in Care

I will try to discuss the general principles in the total care of those who are now or potentially will be our chronically ill. These may be divided into four different phases or components: (1) prevention, (2) diagnosis, (3) treatment, and (4) rehabilitation.

This concept considers the patient as a whole and tends to maintain or improve the physical, mental and vocational powers of the individual so he can be retrained to live and work with whatever potentials he has available.

(1) *Prevention.* Intelligent preventive medicine utilizing all the available medical knowledge can do much to ward off many of the chronic diseases prevalent today.

Why do we shrug off in resignation and pessimism the challenge of the patient growing old? The patient over 50 with aches and pains, changing into a shriveled, weak, kyphotic individual? The dyspeptic old man, querulous, depressed, losing weight, unable to find adjustment to the life of retirement? The patient with mild disease of the urinary tract? The individual with mild disease of the nervous system?

Most minor difficulties can be detected and treated early in life. Impending chronic disability and needless suffering can be prevented. This idea of preventive adult medicine is, of necessity, a new concept in medicine and requires as a basis a periodic health evaluation. We must study those potentially afflicted with degeneration and dysfunction in any aspect of medical disease. This includes the infectious, cardiovascular, metabolic, degenerative, neoplastic and geriatric diseases. There is no longer room for the antiquated medical attitude that considers the patient over 50 with a minor complaint as an "old crock," and a patient over 65 as one who is "simply old" and can be discarded for all intents and purposes as one who has lived his life and needs only T.L.C.

(2) *Diagnosis.* The family physician is the cornerstone of diagnostic service and must be alert to his competency in this field. If he is not cognizant of the opportunities and possibilities of care available, he should at least, once a diagnosis is made, be able to find specialists who are interested in the modern management of the specific chronic disease.

There is much discussion at the present time relative to diagnostic services on a large scale basis. Governmental and private health agencies publicize and furnish these but, on the broad analysis, we are dealing primarily with screening procedures. Examples of these are the activities of the mobile chest x-ray unit, the American Diabetic Association, cancer detection clinics and other screening clinics for specific disease. Once a diagnosis is made there is no assurance that the patient will start proper treatment. Therefore, none of these can surplant the personal relationship between the patient and the family physician,

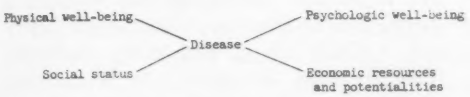
who alone can outline a program of total care.

Although it is extremely wearing, time consuming, unglamorous and economically unrewarding, the physician can no longer procrastinate in the management of long-term chronic disease. His approach must be holistic and evaluate the total life history of these patients—familial, social, dietary, recreational and vocational. The examination must study the nutritional status, alert to early deficiency changes, the cardiovascular state, the metabolic and endocrine situation, the musculoskeletal and the neuropsychiatric state. Laboratory and x-ray studies will help in the search for concomitant diseases. Once this general study is completed and one or more diagnoses reached, a total program must evolve for patient care.

(3) *Treatment.*

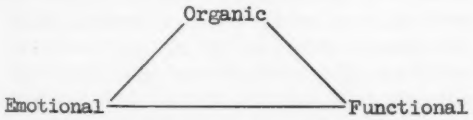
A. Psychologic Adjustment.

The afflicted patient becomes perplexed as he faces an impending disaster which affects every aspect of his life, physical, psychologic, social and economic.



His morale is compromised by pessimism and despondency. His understanding is deluded by the suggestions and advice of well-meaning friends and pseudoscientific literature and advertisements. His logic is vitiated by fads and fancies handed down from mouth to mouth, with no basis of truth. This is compounded by the continued use by many physicians of treatments of limited or useless values.

Within the patient himself there is an interrelated triangle of three factors—organic, functional, and emotional.



Each one of these is closely interrelated to the others and must be evaluated in any program of treatment. Even though we cannot offer a cure to any of these patients, since the pathologic process cannot be reversed, we can offer him an optimistic attitude with which to combat his disease and ameliorate or alleviate his symptoms. At each plateau of the disease the patient must be helped to develop initiative and motivation to get well. He must at all times be an active and integral part of the therapeutic team.

B. General Health Measures.

(a) Proper diet. There is no fad or special diet for any of these diseases. A well-balanced diet will maintain proper nutrition of the entire body. Supplemental vitamins may at times be necessary.

(b) Anemia, once the cause is found, must be combated with proper hematinic substances or transfusions when necessary.

(c) Inasmuch as the patient with chronic disease is very much concerned with his bowel habits, proper elimination must be maintained for the patient is "bowel conscious." Too frequent stools as well as constipation can be a cause of alarm. This enhances a proper psychologic adjustment.

(d) Prevention and management of any concomitant infections are necessary since these may aggravate the chronic disease.

(e) Drugs to stimulate appetite and improve nutrition are often required. Fortunately many are now available.

(f) Elimination of obvious foci of infection. Removal of teeth and tonsils indiscriminately merely adds to the discomfort of these patients, for once the normal good teeth are removed, many times the stimulus to proper mastication of food is decreased. Moreover, many patients never adjust to dentures.

C. Control of Pain.

Drugs used in the control of pain should start with the simplest, such as the salicylates. Only when these fail should more potent drugs be used. Narcotics should be restricted only to the most severe and terminal cases, as in malignancy.

D. Therapy with specific drugs should be used when indicated. However, too often the patient is treated with one of the newer "miracle" drugs in the hope that he will have a dramatic improvement. But are we performing these miracles for him? Or are we adding new disease processes to those already existant? Most of these new drugs are two-edged swords which may help on the one hand and stimulate reaction on the other. Therefore, before using any of these, we must determine

the feasibility of their actions by answering three basic questions:

(a) Is this drug indicated for the condition?

(b) What do I expect this drug to do to and for this patient?

(c) What side-effects can I expect to produce in the patient?

Unless all three questions can be answered in favor of the patient, the drug must be withheld.

E. Physical Medicine. It is impossible to treat chronic disease in a hospital over a long term. Therefore, an adequate program of treatment at home must be instituted. In physiotherapy the two major considerations are heat and exercise. These modalities can be taught to the family. Where there is a Visiting Nurses Association and physiotherapist the program is facilitated. The nurse can evaluate the home situation, set up safety devices in the home and teach the prescribed form of heat and exercise.

The types of heat which can be used are variable, but the preferred ones are radiant heat lamps, moist heat packs, whirlpool baths, warm tub baths, contrast baths and paraffin baths. Though heating pads are the most available they are the least efficient. The therapeutic effect of heat is analgesic and anti-inflammatory and should never be used as the only treatment.

Exercise is the main type of therapy to be taught. Heat and drugs merely prepare the patient for a proper program of exercise. Joints must be moved, muscles must be strengthened. Such cases must be carefully supervised and exercise must be balanced with periods of rest. Too long periods of rest lead to weakness, and too arduous exercise leads to muscle pain and spasm. Therapeutic exercises may be divided into categories according to the muscle function sought.

(a) Strengthening exercises lead to power of muscle and increased strength.

(b) Stretching exercises produce an increase in the elasticity and the ability to contract and relax muscles.

(c) Coordination exercises help to develop purposeful smooth motion.

Each type is important and one or another must be stressed with each disease entity.

(4) *Rehabilitation.* From the time the patient is first seen, the object in mind must be to improve him to his maximum potentialities within the limits of his capabilities, physical, mental, social and vocational. The program must be a realistic one from the start. The objects of such a program of rehabilitation are as follows:

A. To prevent deformities or minimize them if they are present.

B. To retrain the patient in the activities of daily living (A.D.L.).

C. To retrain the patient in recreational and occupational therapy activities.

D. To retrain the patient in substitute skills if he is unable to return to normal activity.

E. To retrain the patient for vocational activity.

(a) The prevention of deformities should begin from the first visit. If any are present they should be treated promptly and vigorously to minimize them. The use of braces, canes, crutches, walkers, wheel chairs, etc., must be available.

(b) Whenever disabilities are present, a program to retrain the patient in the Activities of Daily Living should be instituted. This includes the ability to feed, dress, bathe, communicate and care for one's self.

(c) Recreational facilities and occupational therapy should be available. These activities give patients confidence and often start them on the road to improvement.

(d) Retraining patients in substitute skills compatible with the patient's disabilities helps to show them they can learn new activities.

(e) Finally, many patients can be retrained in their own or new vocational fields.

Much has been done to teach the disabled homemaker the proper placement of equipment and appliances to facilitate their use with minimal effort. These educational methods have resulted in greater prevention of accidents. Tub and shower grab-bars, nonslipping rugs and low storage shelves are essential. All interested in this field should read Dr. Rusk's excellent articles and book on Self-Help Devices for patient.

The Role of the Nurse

In this day of specialization, nursing has become more restricted, and nursing care is confined to nonadministrative nurses and

nurses' aides. The average doctor knows little or nothing about the daily and hourly needs of the ailing patient, let alone the fundamentals of basic nursing care. We rely with such implicit trust in the nurses that we do not even write orders on these fundamental items. We are indeed fortunate when we can call on the Visiting Nurses Association to send a nurse to the home to instruct the patient and his family.

But there is more than just depending on the nurse for the fundamental care of the patient with which you are all familiar. The nurse is one of the chief links in the process of total rehabilitation. She must keep the patient not only well cared for, but also optimistic and convinced of the rewards of perseverance. To do this, she must be convinced of the unquestioned fact that something can be done. No matter how handicapped the patient, he can be helped at least to regain some of the activities of daily living and lead a more comfortable and independent life.

In general, the nurse's role consists therefore of the following:

1. To aid in the psychologic adjustment of the patient and his family to the disease. Teach them to live with the disease and follow directions optimistically.

2. To assist the family in understanding the rudiments of care with maintenance of cleanliness, both of the patient and of the surroundings. Rooms should be well-lighted, well-aired and quiet.

3. To assist in the evaluation of the program of home care designed for the comfort of the patient. Many of the accepted teachings must be modified or disregarded. Beds should be at a level for the patient's comfort and not for the attendant. The mattress should be adequate for prolonged stay in bed eliminating pressure points. A foam rubber mattress on a firm base is good. There should be a foot board to prevent pressure by the covers. Sleeping schedules should be adjusted to the patient's needs and practices. Comfortable garments or night gowns should be worn so the usual pressure ties of the hospital "johnny" is eliminated.

Baths should be given in a shower, or with the patient seated on a cross board on the tub. When no other method is feasible bed baths may be given, but the patient should assist actively. This is a good form of exercise. Bedside commodes or bathroom privileges are necessary. Eliminate the bed pan. Feeding time should be according to the patient's desires and schedule, and food should always be attractive.

4. The administration of medication with alertness for any abnormal allergic or toxic manifestation is essential.

5. To apply and teach the technics of physical therapy as ordered. Demonstrate the technic of exercises and stimulate the patient to early movement to maintain muscle tone and prevent deformities. When possible to take the patient out into the sunlight and fresh air to perform the exercises. Though these do not have any remedial effect they produce an excellent mental tonic and psychologic boost.

6. To help set up and stimulate levels of achievement compatible with the patient's physical and emotional capacities.

Conclusion

Less than 20 years ago more than 75% of a doctor's time was occupied with the care of patients with acute diseases. With the discovery of sulfa drugs in the 1930's, then penicillin, followed by other antibiotics, the victory against acute infectious diseases became a reality.

Today the conquest of these diseases has advanced greatly, and with new antibiotics further success is assured. With this there has come an increasing span of man's life. Man now lives to develop chronic disease and the degenerative diseases of aging.

Chronic diseases produce problems that are complex and ramify into all spheres of existence, psychologic, sociologic and economic. Treatment must, therefore, extend beyond the scope of the physical limitations and include the total disability.

Though there will be no dramatic cures, the fundamentals of care are known. We must enlist the services not only of the doctor and nurse, but also of psychologists, social workers, vocational counselors, physical therapist, occupational therapist, recreational therapist, and other counseling groups.

The goal in this changing concept of chronic disease is clear: to return the patient to his greatest potential within the limits of his capabilities.

Discussion (Abstract)

Dr. T. Paul Haney, Tulsa, Okla. The Cooperative Program for Care of the Abnormally Disabled by Dr. Andelman is very real and practical. As he has pointed out, this group of people is increasing at an alarming rate in our population. Men like Dr. Andelman can do just so much, and if there is a man like him in every large city they alone can only scratch the surface in this field. In planning this part of the program, it was my sincere hope that general practitioners throughout the South would become more interested and participate more actively in care for the chronically ill.

This part of the physician's practice has very little amazing results to offer, but when pursued continuously, as Dr. Andelman has outlined, some of the greatest satisfaction can come to the physician.

Even if *all* general practitioners were most interested in this program, they could not succeed alone. There must be a cooperative program between the welfare department, the public health nurse and the physician. In our county, the public health nurse is the visiting nurse and I shall discuss activities of the two groups as activities of the public health nurse. Dr. Andelman has shown, in Tulsa County, how the public health nurse can enhance the work with chronically ill patients. This can be true throughout the country if private physicians will work with the public health nurse as Dr. Andelman and other physicians in Tulsa County are doing.

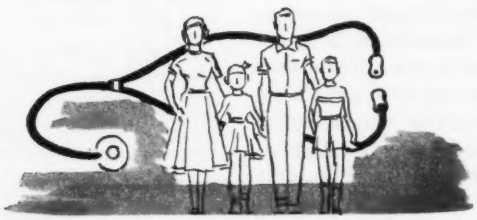
When the private physician becomes acquainted with the services available to him and his patient by the public health nurse, he will find that she wants to be and can be a real partner in all of this work. This will cost the private physician nothing except a little time to instruct the public health nurse concerning the treatment he would have her do.

If the public health nurse in any community is not doing the work of the visiting nurse today, I am sure that a conference with your state and local health officers would result in this most desirable association. In all the work done by the public health nurse in Tulsa County, the family physician is the cornerstone and upon him depends the extent and competency of a program in this field. If the family physician is not familiar with the operations and possibilities of the care available to him and his patients, it is imperative that he learn about this and all other services available to his patients. If you, as physicians, become interested in this cooperative program with the public health nurse, it will become available to you, I am confident.

As Dr. Andelman has pointed out, it is impossible to treat chronic diseases in a hospital over a long period of time. Therefore, an adequate program of home treatment must be instituted. The public health nurse can do all the things in the home with which you have become so familiar in your hospital practice. Ofttimes you will find that these things can be done with relatively little expenditure for setting up facilities and methods of care. Frequently it is simply a matter of instructing the nurse in the type of treatment or in the form of exercise you wish the patient to be taught.

The important point I want to make in this discussion is the end result you wish to obtain for your patients. Rehabilitation, if possible, can be had in any instance in the cooperative program we have discussed. If, in the rehabilitation, the patient can have alleviation of any of his painful inconveniences and worrisome symptoms his problems will be solved.

I urge you as physicians to return from this meeting to use your public health nurse more if you have been accustomed to using her in this field, and if not so accustomed to make yourself acquainted with what is available. If the service you desire is not available, I believe you can, with very little effort on your part, make such valuable assistance available in your community.



Consistency in the Psychologic Reaction to Mescaline

T. W. RICHARDS, Ph.D., *New Orleans, La.*, and
IAN P. STEVENSON, M.D.,† *Charlottesville, Va.*

Intoxication with this alkaloid is characterized by changes in perception and thinking. The authors have studied the consistency of reactions to this intoxication in the same person.

THIS STUDY attempts to demonstrate the degree to which persons receiving mescaline on 2 separate days are consistent in their reaction to the drug. It is generally assumed that the drug induces in almost any person some degree of psychosis-like behavior and experience. How valid is this assumption? Will a previous experience with the drug alter the individual's subsequent reaction to it?

In an attempt to answer these questions, behavior was rated by one of us (I.P.S.) on 2 separate days during which each subject was given mescaline.

On the basis of previous discussion, it was decided to rate the following variables on an eight point scale:

†From the Department of Neurology and Psychiatry, University of Virginia School of Medicine, Charlottesville, Va., and the Department of Psychiatry and Neurology, Louisiana State University School of Medicine, New Orleans, La.

This work was supported by a grant from the Scottish Rite Schizophrenia Research Committee of the National Association of Mental Health.

1a	Anxiety (before administration) Tense, tremulous, fearful, obviously upset	vs.	Calm, controlled, relaxed
1b	Anxiety (after administration of drug) Tense, tremulous, fearful, obviously upset	vs.	Calm, controlled, relaxed
2	Mood Severely retarded emotionally	vs.	Euphoric, expansive
3	Communicativeness Good contact with experimenter, easily interacts	vs.	No contact with environment
4a	Imagery and Fantasy No imagery apparent	vs.	Highly impressive visual and/or other images
$4b_1$	Direction of Attention Completely egocentric: outer environment no concern	vs.	Oriented entirely toward outer environment
$4b_2$	Fixation of Attention Distractible, easily diverted	vs.	Completely absorbed in subjective experiences
5a	Perception of Body Experiences body in usual way	vs.	Hands or skin or legs seem abnormal
5b	Perception of objects in external enivronment Hallucinated	vs.	Intact
6a	Depersonalization Exaggerated sense of self	vs.	Loss of control of thoughts
6b	Insight into current situation Aware of role in real situation	vs.	Denial of reality of life situation
7	Paranoid trends Complete acceptance of own responsibility	vs.	Suspicious, blames others entirely for present situation
8	Sensitivity to reduced control Indifferent to situation	vs.	Panic

Subjects for the study were 15 medical students and residents and one graduate student in psychology. All 16 subjects were volunteers.

Results

In table 1 appear the mean ratings for the group of 16 subjects for the first and second administrations of mescaline; in the third column appear *t* values for the significance of differences. Any *t* value of 1.8 or more should be considered seriously as indicating a significant difference.

From table 1 it may be inferred that the subjects in their second experience with mescaline were significantly less anxious prior to the administration of the drug than they were the first time. During mescaline on the second occasion they were more communicative and showed a greater degree of depersonalization and distortion of perception of their environment. For other variables they showed no significant change between trials.

Consistency for individuals in the group between trials is best shown by the degree of intercorrelation between sessions. Following are Pearson coefficients of such correlation:

1a	Anxiety (before)	.46
1b	Anxiety (during)	.47
2	Mood	.08
3	Communicativeness	.22
4a	Imagery and fantasy	.05
$4b_1$	Attention: direction	.59
$4b_2$	Attention: fixation	.34
5a	Perception of body	.01
5b	Perception of environment	.47
6a	Depersonalization	.72
6b	Insight	.63
7	Paranoid trends	.14
8	Sensitivity	.47

With a population of 16 cases, a coefficient should be about .50 at the 5% level of expectancy, and about .62 at the 1% level.

It is seen that there is greatest consistency for *depersonalization, insight* and *direction of attention.* There is no consistency for *mood, communicativeness, imagery* and *fantasy, perception of body* and *paranoid* trends. There is a fair degree of consistency for *anxiety,* both before and during the experiment and for *perception of the environment; fixation of attention* shows a slight consistency.

TABLE 1

	Variable	Mean Experiment 1	Mean Experiment 2	*t*
1a	Anxiety (before)	2.6	2.0	1.8
1b	Anxiety (during)	2.0	2.2	0.3
2	Mood (elation)	5.9	5.6	0.2
3	Communicativeness	5.1	6.2	2.1
4a	Imagery and fantasy	5.7	5.3	1.3
$4b_1$	Attention (inward)	5.9	5.9	0.0
$4b_2$	Attention (strong)	5.2	5.1	0.3
5a	Body perception (distorted)	4.7	5.1	1.0
5b	Environmental perception (distorted)	5.3	5.9	2.0
6a	Depersonalization	4.4	5.1	2.3
6b	Insight (poor)	2.1	2.0	0.0
7	Paranoid	2.0	1.8	0.0
8	Sensitivity (panic)	3.6	3.4	0.3

Mean ratings on 13 variables for 16 subjects who were given mescaline in 2 experiments, and the *t* values for the significance of differences between them. Capitalized term designating variable indicates higher score.

Summary and Conclusion

As a group, these 16 subjects seem less apprehensive at the beginning of the second experiment, and during it they were more communicative toward the experimenter. They showed greater depersonalization and greater distortion of perception of the environment.

As regards individuals in the group, it was found that subjects who are high (or low) on depersonalization, insight and direction of attention remain so in the second experiment.

EDITORIALS

MEDICINE AND THE WELFARE STATE

Recent news items have made much of what one community in New York has done in an effort to stop the welfare state. "Bulldozer" tactics were used and much interest was developed. In 1957, Dr. Bruce B. Blackmon, and other members of the medical profession in Harnett County, North Carolina, a county with an agrarian population of 48,236, through the cooperation of their county welfare board, set up a study which brought out the fact that it was easy for nonenergetic people to get on the welfare rolls but that it was hard to get them off. Two approaches were used in the study: first, a review of old medical records; second, a physical examination by a team of three physicians of all new applicants who applied to get on the welfare rolls for medical reasons. The results were astounding.

A review of all medical records on file was begun. (It should be emphasized that only the medical records were made available to the committee.) To date, two thirds of the records have been reviewed. Twenty-six per cent of this group of welfare recipients appeared to be questionable as being classified as totally and permanently disabled. One client had been drawing a check since 1950 because of cancer. There were three possible medical explanations for this instance:— first, there had been no cancer; second, the cancer had been cured; or third, the patient was dead. The answer turned out to be the second possibility. For 10 years this patient, who had had a cancer which had been detected early, had been treated and cured, all as a welfare recipient, and had been drawing a monthly check as a "cancer victim." Of the 26% questionable files, one half or 13% of the original files showed the recipient not to be disabled to the extent of eligibility to receive welfare checks.

An alphabetically rotating committee of three physicians from the Harnett County Medical Society was organized to examine each new applicant who was applying for aid for medical reasons. All persons making application for welfare for medical reasons were told to report to the County Health Department on the 4th Friday of each month at a given time, at which time the team of three physicians examined each patient and formulated a combined opinion concerning disability of the patient. All this work was done gratis. Since this system was adopted, no patient has been examined in a physician's office in Harnett County for welfare disability. The system has resulted in a tremendous saving of time for the individual physician, and has guaranteed to each applicant that he will have the benefit of the best judgment of three physicians without charge. For the county taxpayer it has provided protection from applicants being put on the roll because an individual physician has been placed under pressure or because the recipient is malingering. Shortly after the procedure was initiated, it became evident that applicants who were possible malingerers were going out of the county to as far as 50 miles from home to have their physical examinations done. The welfare department solved this problem by accepting reports from no one other than the local review team or one of the three teaching institutions in the State or the V. A. Hospitals.

Results: By a review of two thirds of the medical files which looked doubtful, 30 welfare cases were terminated. The last one third of the files had not been reviewed as yet; two thirds were reviewed because it was time for the recipient to have his periodic re-examination as required by the welfare regulations. Each of these was seen in due course of time and screened as they came before the review team. Although the exact figures are not available, it is assumed that the same percentage will hold as for elimination of the 30 recipients who have been removed by the screening procedure. The average check received by recipients in Harnett County under the aid to the permanent and totally disabled category is $46.00. This figure multiplied by 30 equals $1,380.00 saved for the taxpayers monthly, or $16,560.00 annually. This does not take into consideration those who apply but who, when they learn they will have to appear before the local medical team, withdraw their

applications or fail to show up for the examination. From the patient's point of view, by having a scheduled time each month, every applicant is assured of an adequate examination without cost and without competing with sick patients and patients in labor for a few minutes of his family physician's time to "get a form filled in." From the physician's point of view, he knows several months in advance when his tour of duty comes up for one-half day per month for three consecutive months to serve on the medical review team. In the meantime he does not have to stop seeing sick patients in the middle of a busy day just to "fill in some more forms." A physician has now been appointed on the Harnett County Welfare Board. A mutual feeling of cooperation has developed between the Welfare Board and the Medical Society. The physicians have become more tolerant of the Welfare Department and the Welfare Department has become keenly aware of the presence of malingering, and together they are saving a small county $16,560.00 annually, and probably making better citizens of malingerers by allowing or forcing them to become self-supporting instead of continuing as parasites on society. Those applicants who are found in need of medical attention can be directed to the proper facilities and gain that great relief of knowing that they are no longer without treatment and that they can resume their normal lives and occupations. The Harnett County program has threatened no one. It has recognized the responsibility of taking care of the needy and may have found one stopgap to help save this country from the horrors of a welfare state.

LENOX D. BAKER, M.D.

VACCINATION AGAINST INFLUENZA—NOW!

The catastrophic influenza epidemic of 1918-1919 has represented in the minds of so many the high water-mark of mortality from epidemic disease, that lesser proportions in the other epidemics have not made an adequate impression upon the profession.

Nevertheless, respect should be tendered the Asian strain of influenza, for it has been no mean contender for the place as "runner-up" in morbidity and mortality in recent years. Since May 1957, when this strain was first recognized, it has represented an epidemic disease with which to reckon. In the first two waves, September through December 1957 and January through March 1958, almost 40,000 excess deaths occurred in the first and 20,000 in the second wave. The second major epidemic, in the first three months of 1960, caused 27,000 excess deaths. Thus, 86,000 deaths over the expected number for the country was caused by the Asian influenza epidemic in a three year period. This does not take into account the increased morbidity which inevitably accompanies such an increase in mortality rate.[1]

The analysis of excess deaths included not only the basic influenza-pneumonia deaths, but took into account deaths in which influenza may have been secondary to other disease. Those over age 65 revealed the highest death rates,—in the first epidemic period a little over 50% of the excess deaths occurred in those over this age, and in the 1960 epidemic 80% of such deaths occurred in the older group. Of the total excess deaths 85% fell into two categories—pneumonia-influenza and cardiovascular-renal disease. The latter category as a cause of death appeared in one half of the 86,000 excess deaths in the three year period.

The analysis of mortality rates in other categories and for pregnant women is detailed in the study from the Communicable Disease Center of the U. S. Public Health Service.[1] As a result of these observations, the Surgeon General's Advisory Committee on Influenza has recently publicized recommendations for vaccination against the Asian strain of influenza. Since reports indicate that the vaccine is 60 to 75% effective, it is urged that vaccination be used in the following groups especially: "(A) Persons of all ages who suffer from chronic debilitating diseases, e.g., chronic cardiovascular, pulmonary, renal or metabolic disorders, in particular: (1) Patients with rheumatic heart disease, especially those with mitral stenosis. (2) Patients with other cardiovascular disorders such as arteriosclerotic heart disease and hypertension, especially those with evidence of frank or incipient cardiac insufficiency. (3) Patients with chronic bronchopulmonary disease, for example, chronic asthma, chronic bronchitis, bronchiectasis, pulmonary fibrosis, pulmonary emphysema,

1. Eickhoff, T. C., Sherman, Ida L., and Serfling, R. E.: Observations on Excess Mortality Associated with Epidemic Influenza, J.A.M.A. 176:776, 1961.

pulmonary tuberculosis. (4) Patients with diabetes mellitus. (5) Patients with Addison's disease. (B) Pregnant women. (C) All persons over 65 years of age."[2]

Furthermore, vaccination is also recommended for those engaged in medical and health services, public safety, public utilities, public transportation, education and communications; as well as for persons in the age groups in which influenza occurs in its highest incidence, namely, from ages 5 to 25 years.

The Surgeon General's Advisory Committee on Influenza has offered the following recommendations:

Dose and Schedule of Vaccination by Age

1. *Adults (i.e., individuals 13 years of age or older):* 1.0 cc. (500 CCA units) should be administered subcutaneously as soon as practicable after September 1 and no later than January 1. Those not previously immunized should receive, if feasible, a second dose of 1.0 cc. approximately 2 months after the first injection.
2. *Children aged 6 to 12 years of age:* 0.5 cc. (250 CCA units) should be administered subcutaneously as soon as practicable after September 1 and no later than January 1. Those not previously immunized should receive, if feasible, a second dose of 0.5 cc. approximately 2 months after the first injection.
3. *Children 3 months old to pre-school age:* Initial doses of 0.1 to 0.2 ml. (50 to 100 CCA units) should be administered subcutaneously on two occasions, separated by one or two week intervals. A "booster" inoculation of the same strength should be given, if feasible, 2 to 3 months later. Preferably the schedule of vaccination should be completed by January 1.
4. *Persons previously immunized with polyvalent vaccine:* Each fall, prior to January 1, persons previously immunized with polyvalent influenza virus vaccine should be re-inoculated with a single dose according to the following schedule:

   Children 3 months old to pre-school age: 0.1 to 0.2 ml.

   Children aged 6 to 12 years: 0.5 ml.

   Adults: 1 ml.

2. Surgeon General's Advisory Committee on Influenza: Recommendations for Vaccination Against Influenza in the Civilian Population, 1961.

SOUTHERN MEDICAL NEWS

ALABAMA

Dr. Stanley S. Kahn, Birmingham, has been elected a Fellow of the American College of Physicians.

Dr. Howard L. Holley, University of Alabama Medical Center, has been appointed a member of the Fourteenth and Fifteenth Rheumatism Review Committee of the American Rheumatism Association and has been named to serve on the Arthritis Training Grants Committee of the National Institutes of Health.

ARKANSAS

Dr. Sam J. Kuykendall, Little Rock, is a Fellow of the American College of Chest Physicians.

A Bentonville physician, Dr. R. M. Atkinson, has been advanced to an Associate Member of the International College of Surgeons.

Two young physicians, Drs. Billy J. Jordan and Charles Hicks, have opened their practice at the Hamburg Clinic in Hamburg. Both are also new members of the Ashley County Medical Society.

DISTRICT OF COLUMBIA

The Washington Academy of Surgery has elected the following officers: Dr. Garnet W. Ault, President; Dr. Saul Schwartzbach, Vice-President; Dr. Brooks G. Brown, Secretary-Treasurer; and Dr. Frank J. Sanzaro, Assistant Secretary.

Officers of the District of Columbia Chapter of the American Academy of General Practice include: Dr. Ernest H. Aschenbach, President; Dr. W. Robert Perkins, Vice-President; Dr. Russell M. Tilley, Secretary; and Dr. Millard F. Ottman, Treasurer.

Dr. C. Willard Camalier, Jr., was recently appointed a member of the three member Medical Advisory Committee to the Board of Directors of the National Association of Blue Shield Plans.

Dr. Reginald S. Lourie, Chairman of the Department of Psychiatry at Children's Hospital, was named President-Elect of the American Academy of Child Psychiatry.

Officers of the Section on Radiology of the Medical Society of the District of Columbia are: Dr. John S. Hashim, Chairman; Dr. Alfred A. J. Den, Chairman-Elect; and Dr. William E. Sheely, Secretary-Treasurer.

Dr. Hugh H. Hussey, Dean of the Georgetown University School of Medicine, has been elected Chairman of the Board of Trustees of the American Medical Association.

Col. Robert C. Hunter has succeeded Col. Conn L. Milburn, Jr., as Executive Officer of Walter Reed General Hospital. Col. Milburn has been appointed Director of the Walter Reed Army Institute of Research.

Dr. Frank E. Wilson, Executive Vice-President of the Joint Blood Council, has been designated as Chairman of the Advisory Council on Reserve Affairs by Lt. General Leonard D. Heaton, the Army Surgeon General.

Dr. Thomas W. Mattingly became a founding member of the Association of University Cardiologists at its recent organizational meeting.

The Kentucky State Medical Association has presented awards to Mrs. Eva Ray Wunderlich, left, for meritorious service in public health by a layman, and to Dr. A. Clayton McCarty, right, for distinguished service. Dr. William H. Bizot, center, made the presentations during the recent annual meeting of the KSMA in Louisville. In addition to his honor, Dr. McCarty, who is President-Elect of Southern Medical Association, has been named President of the American Geriatrics Society and has been chosen First Vice-President of the American Therapeutic Society.

Dr. Samuel Zola is the new Senior Attending Surgeon at Providence Hospital.

Dr. Maurice Protas has been elected to the Council of the American Diabetes Association. Dr. Protas was also elected Chairman of the Assembly of State Governors and Affiliate Delegates of the ADA.

Dr. Robert C. Hecker has been elected Chairman of the Physicians' Advisory Committee to the Greater Southeast Community Hospital.

Dr. J. Winthrop Peabody, Jr., is a Fellow of the American College of Chest Physicians.

FLORIDA

The University of Miami School of Medicine, Section of Thoracic and Cardiovascular Surgery, announces postgraduate cardiac surgical colloquia for the year 1961-62. The November 1961 program will feature Dr. Howard L. Gadboys, Clinical Assistant Professor of Surgery, University of Miami School of Medicine, and the topic "Homologous Blood Syndrome during Clinical Cardiopulmonary Bypass." The conferences will be held from 10:30 a.m. to 12 noon at Jackson Memorial Hospital in Miami. For further information and a complete schedule of the program contact Dr. Robert S. Litwak, Chief, Section of Thoracic and Cardiovascular Surgery, University of Miami School of Medicine, Miami, Florida.

Dr. George H. Garmany, Tallahassee, and Dr. Alpheus T. Kennedy, Pensacola, have been appointed members of the State Board of Medical Examiners by Governor Farris Bryant.

Dr. Perry A. Sperber, Jr., Daytona Beach, has been made a Fellow in the American Association for the Advancement of Science.

Dr. Robert J. Brown, Jacksonville, has been elected to the Board of Directors of the Jacksonville Blood Bank.

Officers of the Florida Radiological Association are: Dr. John P. Ferrell, St. Petersburg, President; Dr. Alfred G. Levin, Miami, President-Elect; Dr. Ivan Isaacs, Jacksonville, Vice-President; Dr. Richard S. Shapiro, Miami Beach, Secretary; and Dr. Marvin V. McClow, Jacksonville, Treasurer.

GEORGIA

The Richmond County Medical Society, Augusta, announces the Augusta Postgraduate Medical Assembly, April 2-4, 1962. The registration fee of $15.00 covers the sessions, which will be of general interest, and a cocktail party. Since the Assembly coincides with practice rounds of the Masters Golf Tournament, early registration is urged. Registration will be limited. Write: Dr. Julius T. Johnson, Chairman, Postgraduate Medical Assembly Committee, P. O. Box 3323, Augusta, Georgia.

The Medical College of Georgia has announced the following faculty promotions for the year 1961-62: Dr. Floyd E. Bliven, Professor of Surgery (Orthopedics); Dr. John R. Fair, Professor of Surgery (Ophthalmology); Dr. Frank P. Anderson, Associate Professor of Pediatrics; Dr. Harold S. Engler, Associate Professor of General Medicine; Dr. Enon C. Hopkins, Associate Professor of Medicine; Dr. James A. Kemp, Assistant Professor of Medicine; Dr. Winford H. Pool, Jr., Assistant Professor of Radiology; Drs. Iverson Bryans and William Thurmond, Clinical Professors of Obstetrics and Gynecology; Drs. William S. Boyd, John Persall, and Walter G. Watson, Associate Clinical Professors in Obstetrics and Gynecology; and Dr. Gordon Walters, Clinical Instructor in Medicine.

Dr. Gabriel D'Amato, Savannah, has accepted the position of Associate Professor of Psychiatry at the Medical College of Georgia.

Dr. Eustace Allen, Atlanta, has been elected Vice-President of the American Medical Association.

Dr. L. H. Griffin, Claxton, has been installed as President of the Alumni of the Medical College of Georgia.

Dr. W. G. Elliott, Cuthbert, is President of the Georgia Chapter, American College of Chest Physicians.

Dr. James W. Purcell, Covington, has been named a member of the International College of Surgeons.

Officers of the Georgia Pediatric Society are: Dr. John T. Leslie, Decatur, President, and Dr. Joseph Patterson, Atlanta, President-Elect.

Dr. Pete Inglis, Marietta, was recently named President of the Cobb-Douglas-Paulding Tuberculosis Association.

Dr. Alfred Colquitt, Jr., Marietta, has been elected a member of the Board of Directors of Cobb Exchange Bank.

Dr. Richard Gray, Rome, has been named a Lieutenant Governor of Optimist Club International.

The President-Elect of the Georgia State Obstetrical and Gynecological Society is Dr. Tom A. Dover, Athens.

Dr. Nanette Kass Wenger, Instructor in Medicine at Emory University School of Medicine in Atlanta, has been awarded the Outstanding Achievement Award by Hunter College in New York City.

Dr. A. H. Letton, Atlanta, has been elected Chairman of Region III of the American Cancer Society.

Two Emory University faculty members are members of the American Gastroenterological Association. Dr. Spalding Schroder has been advanced from an Associate Member to a full Active Member and Dr. Julius Wenger has been named an Associate Member.

Dr. J. Frank Walker, Atlanta, is a member of the Board of Directors of the Peachtree Civitan Club.

Dr. Irving L. Greenberg, Atlanta, was recently re-elected to serve a second term as President of the Atlanta Jewish Community Council and installed as President of the Atlanta Chapter of the Phi Delta Epsilon National Medical Fraternity Graduate Club.

KENTUCKY

Dr. Carroll L. Witten, Louisville, is the only practicing doctor on a 16 member committee named by the American National Red Cross to rewrite its home-nursing textbook. Dr. Witten is an Associate Councilor from Kentucky to Southern Medical Association.

Dr. George J. Van Besien, Louisville, has been appointed Director of the Out-patient Clinic of the Veterans Administration regional office in Louisville.

Dr. Frederick Edward Kratter, formerly staff psychiatrist at Pineland Hospital, Pownal, Maine, has been named Clinical Director of Western State Hospital in Hopkinsville.

The University of Louisville School of Medicine has announced several changes in the faculty. Dr. J. Murray Kinsman, Dean of the School of Medicine, has been given the additional title of Director of Hospital Relations. Dr. Kenneth F. Keller has been appointed as Instructor on Microbiology. Two faculty members have been promoted: Dr. Sidney Roston from Instructor to Assistant Professor of Medicine, and Dr. Warren H. Dennis from Associate in Physiology to Assistant Professor of Biophysics in the Department of Physiology and from Instructor to Associate Professor in the Department of Community Health.

The American Academy of Pediatrics has elected three Louisville physicians as Fellows: Drs. William W. Johnson, John Doyle, and J. Kenneth Harris. Dr. Johnson was also elected a member of the Section of Surgery of the Academy.

Officers of the Kentucky Pediatric Society are: Dr. Murvel C. Blair, Frankfort, President; Dr. Noble T. MacFarlane, Lexington, Vice-President; and Dr. Joseph Liebman, Frankfort, Secretary-Treasurer.

Dr. Kenneth B. Moore has joined the staff of the Veterans Administration Hospital in Lexington where he will limit his practice to psychiatry.

Dr. Carl H. Fortune, Lexington, a graduate of Transylvania College, has received an honorary degree of Doctor of Science from that school.

Dr. Alfonso V. Wilwayco, Franklin, has been appointed Health Officer for Logan, Simpson, and Allen Counties.

Dr. Wilford L. Cooper, Lexington, was recently chosen President-Elect of the Ohio Valley Proctologic Society. Dr. Marvin A. Lucas, Louisville, is a member of the Executive Council of the Society.

Dr. Alvin B. Mullen, Waverly Hills, former Medical Director of the Waverly Hills Sanatorium, has been appointed Director of Tuberculosis Control for Louisville and Jefferson County.

Dr. William R. Willard, Vice-President of the University of Kentucky Medical Center, Lexington, has been named one of 22 members of the Surgeon General's Consultant Group on Nursing.

Officers of the Kentucky Heart Association are: Dr. Marc J. Reardon, Covington, President; Dr. Richard R. Crutcher, Lexington, First Vice-President; and Dr. George W. Pedigo, Jr., Louisville, Vice-President.

Dr. Harry C. Denham, Maysville, has been installed as President of the University of Kentucky Alumni Association.

Dr. Dillard D. Turner, London, has been named Director of Public Health for the four counties of Crittenden, Caldwell, Livingston, and Lyons.

Dr. Mitchell B. Denham, Maysville, has been chosen as Maysville's outstanding citizen by the local high school Hi-Y club.

LOUISIANA

The twenty-fifth annual meeting of The New Orleans Graduate Medical Assembly will be held March 12-15, 1962, with headquarters at The Roosevelt Hotel. Nineteen outstanding guest speakers will present 55 discussions, in addition to clinicopathologic conferences, symposia, medical motion pictures, round-table luncheons and technical exhibits. Following the meeting in New Orleans, arrangements have been made for a clinical tour to the Eastern Mediterranean leaving New Orleans via air on March 16. The itinerary includes visits to Athens, Rhodes, Cairo, Luxor, Jerusalem and Tel Aviv, returning on April 6 to New York. (Optional extensions in Europe may be arranged.) Details of the New Orleans meeting and the tour are available at the office of the Assembly, Room 105, 1430 Tulane Avenue, New Orleans 12, Louisiana.

Dr. J. William Rosenthal, New Orleans, has been awarded the degree of Doctor of Medical Science in Ophthalmology (D.Sc.) from the University of Pennsylvania.

Dr. William Newsom, until recently Director of New Orleans Charity Hospital's Premature Infant Care Program, has been appointed Director of Nutritional Research for the Carnation Company in Van Nuys, California.

MARYLAND

Dr. Frederick A. Holden, Towson, is one of 269 men now serving as Governors of Rotary International.

Dr. Lee B. Mathews, Cumberland, has been named the county physician.

Dr. Leon Eisenberg has been promoted to Professor of Child Psychiatry at Johns Hopkins University School of Medicine.

Dr. Merrill M. Cross, Silver Spring, has been appointed Chairman of the Liaison Committee on National Defense of the American Academy of General Practice.

Dr. Seymour J. Kreshover, Bethesda, Associate Director of the National Institute of Dental Research,

Continued on page 70

BOOKS RECEIVED

Bleeding Syndromes. A Clinical Manual. By Oscar D. Ratnoff, M.D., Associate Professor of Medicine, Western Reserve University School of Medicine. 269 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1960. Price $8.50.

Congenital Malformations of the Heart. Volume II. Specific Malformations. By Helen B. Taussig, M.D. Second Edition, 1,007 pages. Cambridge: The Commonwealth Fund by Harvard University Press, 1960. Price $17.50.

Motor Examination of Peripheral Nerve Injuries. By Y. T. Oester, M.D., Professor of Pharmacology, Stritch School of Medicine, Loyola University, Chicago, and John H. Mayer, Jr., M.D. 89 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1960. Price $5.50.

The Pathology of Cerebral Palsy. By Abraham Towbin, M.D., formerly Associate Professor of Pathology, Ohio State University. 187 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1960. Price $8.00.

The Transplantation of Tissues and Organs. By Michael F. A. Woodruff, M.D., M.S. (Melb.), F.R.C.S., F.R.C.S.E., F.R.A.C.S., Professor of Surgical Science in the University of Edinburgh. 727 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1960. Price $25.50.

Dynamic Psychiatry in Simple Terms. By Robert R. Mezer, M.D., Assistant Professor of Psychiatry, Boston University Medical School. 162 pages. New York: Springer Publishing Company, 1960. Price $2.75.

Atlas of Anatomy and Surgical Approaches in Orthopaedic Surgery: The Lower Extremity. Volume II. By Rodolfo Cosentino, M.D., Assistant Professor in Orthopaedic Surgery, University of La Plata, Argentina. 264 pages, illustrated. Springfield, Ill.: Charles C. Thomas, Publisher, 1961. Price $14.00.

Instructional Course Lectures, Vol. XVII, 1960. Edited by Fred C. Reynolds, M.D., St. Louis. 406 pages, illustrated. St. Louis: The C. V. Mosby Company, 1960. Price $18.50.

Haemopoiesis. Cell Production and Its Regulation. Ciba Foundation Symposium. Edited by G. E. W. Wolstenholme and Maeve O'Connor. 466 pages. Boston: Little, Brown & Company, 1960. Price $11.00.

Clinical Disorders of the Pulmonary Circulation. By Dr. Raymond Daley, Dr. John G. Goodwin and Dr. Robert E. Steiner. 364 pages, 133 illustrations. Boston: Little, Brown & Company. Price $14.00.

Valvular Disease of the Heart in Old Age. By P. D. Bedford, M.D., M.R.C.P., Consultant Physician to Cowley Road Hospital, Oxford, and F. I. Caird, D.M., Oxford. 185 pages, 38 illustrations. Boston: Little, Brown & Company, 1960. Price $7.50.

Biology of Pyelonephritis. Edited by Edward L. Quinn, M.D., Physician in Charge, Division of Infectious Diseases, Henry Ford Hospital; and Edward H. Kass, M.D., Associate Professor of Bacteriology and Immunology, Harvard Medical School. Henry Ford Hospital International Symposium. 696 pages. Boston: Little, Brown & Company, 1960. Price $18.00.

Clinicopathological Conferences of the Massachusetts General Hospital. Edited by Benjamin Castleman, M.D., Clinical Professor of Pathology, Harvard Medical School, and H. Robert Dudley, Jr., M.D., Instructor in Pathology, Harvard Medical School. 289 pages. Boston: Little, Brown & Company, 1960. Price $12.50.

The Operations for Inguinal Hernia. By Mark M. Ravitch, M.D., Associate Professor of Surgery, and James M. Hitzrot II, M.D., Resident in Orthopedic Surgery, both of the Johns Hopkins University School of Medicine. 64 pages. St. Louis: The C. V. Mosby Company, 1960. Price $4.00.

Disc Lesions. By E. J. Crisp, M.D., D.Phys. Med. (Lond.), Consultant Physician Emeritus in Physical Medicine, Guy's Hospital, London. 156 pages. Baltimore: The Williams & Wilkins Company, 1960. Price $3.75.

Traumatic Lesions of Peripheral Vessels. By Carl W. Hughes, M.D., Lt. Col., Medical Corps, U. S. Army, Assistant Chief, Department of Surgery and Chief, General Surgery Service, Tripler U. S. Army Hospital, and Warner F. Bowers, M.D., Col. Medical Corps, Chief, Department of Surgery, Tripler U. S. Army Hospital. 191 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1961. Price $8.00.

Recent Advances in Pathology. Edited by C. V. Harrison, M.D., Professor of Morbid Anatomy, University of London Postgraduate Medical School. 451 pages, 140 illustrations. Boston: Little, Brown & Company, 1960. Price $11.00.

Pathogenesis and Treatment of Cerebrovascular Disease. Seventh Annual Scientific Meeting of Houston Neurological Society. Compiled and edited by William S. Fields, Professor and Chairman, Department of Neurology, Baylor University College of Medicine. 556 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1961. Price $15.00.

Kernicterus and Its Importance in Cerebral Palsy. A Conference presented by The American Academy for Cerebral Palsy, New Orleans, La. 285 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1961. Price $8.75.

Surgical Treatment of Intracranial Meningiomas. By Collin S. MacCarty, M.D., Consultant in Neurologic Surgery, The Mayo Clinic. 69 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1961. Price $4.50.

A Biological Basis of Multiple Sclerosis. By Roy L. Swank, M.D., Professor and Head, Division of Neurology, Department of Medicine, University of Oregon Medical School. American Lecture Series. 85 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1961. Price $5.00.

Parkinsonism. Its Medical and Surgical Therapy. By Irving S. Cooper, M.D., Professor of Research Surgery, New York University School of Medicine. 228 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1961. Price $16.50.

Optics. By Kenneth N. Ogle, Ph.D., Head, Section of Biophysics and Professor of Physiological Optics, Mayo Foundation. 259 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1961. Price $8.75.

Light Coagulation. By Gerd Meyer-Schwickerath, M.D., Municipal Eye Clinic, Essen, Professor of Ophthalmology, University of Bonn. Translated by Stephen M. Drance, M.B., F.R.C.S., Associate Professor of Ophthalmology, University of Saskatchewan. 114 pages. St. Louis: The C. V. Mosby Company, 1960. Price $9.50.

Beloved Professor. Life and Times of William Dodge Frost. By Russell E. Frost. 338 pages. New York: Vantage Press, 1961. Price $3.75.

Drugs in Current Use 1961. Edited by Walter Modell, M.D., Associate Professor of Clinical Pharmacology, Cornell University. 154 pages. New York: Springer Publishing Company, Inc., 1961. Price $2.25.

Cutaneous Manifestations of the Benign Inflammatory Reticuloses. Edited by Samuel M. Bluefarb, M.D., Associate Professor of Dermatology, Northwestern University Medical School, Chicago. American Lecture Series. 402 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1960. Price $14.00.

The Chemical Basis of Clinical Psychiatry. By A. Hoffer, M.D., University Hospital, Saskatoon, Saskatchewan, and Humphry Osmond, M.R.C.S., D.P.M. Psychiatric Research Division, Saskatchewan Hospital, Weyburn, Saskatchewan. American Lecture Series. 256 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1960. Price $8.50.

Quantitative Cellular Haematology. By J. M. Yoffey, M.D., F.R.C.S. (Eng.), Professor of Anatomy, University of Bristol, England. American Lecture Series. 118 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1960. Price $5.50.

Progress in Clinical Surgery, Series II. By various Authors, edited by Rodney Smith, M.S., F.R.C.S., Surgeon, St. George's Hospital, London. 321 pages, 110 illustrations. Boston: Little, Brown & Company, 1961. Price $11.50.

Cancer Chemotherapy. Prepared by the Staff of the University of Texas, M. D. Anderson Hospital and Tumor Institute, Texas Medical Center, under the direction of R. Lee Clark, Jr., M.D., American Lecture Series. 244 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1961. Price $10.50.

A Synopsis of Physiology (Rendle Short). Edited by C. C. N. Vass, M.Sc., Ph.D., M.B., Ch.B., Reader in Physiology in the University of London. Fifth Edition. Baltimore: Williams & Wilkins Company, 1961. Price $8.00.

Chemistry of Drug Metabolism. By William H. Fishman, Ph.D., Tufts University School of Medicine, Boston. American Lecture Series. 211 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1961. Price $10.50.

BOOK REVIEWS

Slice Reconstructions of Human Cerebral Sections

By Wendell J. S. Krieg, Ph.D., Professor of Anatomy, Northwestern University Medical School. Illustrated. 1960. Price $1.00.

Dr. Krieg has produced with much loving labor a pair of volumes both of which complement each other and will supplement his well-known *Functional Neuroanatomy*. The plates of cerebral sections are to be incorporated in the next edition of his basic text; the multicolored representations of brain stem levels will exist intact as a laboratory section review, which may be scanned with profit quite apart from slides.

The enhancement of morphologic appreciation of the brain stem by hand-printing in eight colors is pleasant and undoubtedly will supply further stimulation to the beginner to break the ice in a subject that ordinarily seems to automatically short-circuit the most hardy. It will not replace repetitive review, but unlike other more diagrammatic attempts has not utilized color in place of accurate anatomy and can be strongly recommended for this purpose.

The series of cerebral serial coronal sections was devised chiefly to illustrate the internal fiber complexes running below the cortex toward their lower connections. The drawings are meticulous, quite obviously represent untold labor, and represent excellent research. The author points out that it has been "usual to regard the white matter . . . as an undifferentiated felt work" and that "close study of this series of drawings will be repaid with a fuller understanding of cerebral anatomy than it is possible to obtain anywhere else today." This enthusiasm of the neuroanatomist has merit, but the clinician may reasonably leave his knowledge in this particular area in less depth than would be ideal from the author's viewpoint.

Studies on Vertebrate Neurogenesis

By Professor Santiago Ramon Y. Cajal, Faculty of Medicine, University of Madrid, translated by Lloyd Guth, M.D., National Institutes of Health, Bethesda. 423 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1960. Price $13.50.

This book gives a clear and methodic description on neurogenesis by a scientist of distinction, Cajal; its pages represent the pioneer work of this branch of the science. On the whole, the book is very well presented, well translated, easy to read, thanks to the careful work of Dr. Lloyd Guth. The illustrations are classical, of course, and the book is well organized. The reader will appreciate this contribution because he will find in it the basic information helpful to the understanding of some of the complex problems in neurogenesis. There was a real need, as Dr. Lloyd Guth says, for such a book in a field that is going to suffer some changes with the advent of new technical elements.

The personal contribution of Cajal in Nervous System was decisive having changed completely in 1888, the current ideas about its constitution and compiling in 50 years of indefatigable work an immense body of knowledge. This knowledge which Cajal and his associates and many others have handed down is a wonderful heritage. In their older work very few errors have been proved; most of it has stood the tests of the following years. Those pioneer studies were complete and little has been added to them for 60 years. Modern technical advances have only added details.

The electron microscope, cytochemical and enzyme stains are challenging the older disciplines—using Dr. Greenfield's words—and a complete review of the older concepts has to take place. But these new investigations must start from a base and that basic knowledge is found in this book regarding neurogenesis.

Cirrhosis of the Liver

By Martin Seler Kleckner, Jr., M.D. 726 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1960. Price $24.50.

The author has undertaken a Herculean task of reviewing and discussing the morphogenetic concept of cirrhosis, the pathologic and the clinical features of the various types of cirrhosis, and the physiologic aberrations consequent to cirrhosis. It is, of necessity, incomplete and scanty in places. Nevertheless, the various chapters are well referenced and arranged in such a manner that they may be of ready assistance to the busy practitioner. This is a review text with numerous illustrations and tables that should make it especially attractive to those not initially well versed in manifestations of cirrhosis. Unfortunately there are several editorial errors which detract from the quality and a number of the figures seem superfluous.

Since it is directed toward the practicing clinician, its very superficial approach to the physiology and pathophysiology of the liver with regards to fat metabolism, protein metabolism, and carbohydrate metabolism, may be excused. Its sections on therapeutics are by and large clear and well directed although some of the currently significant aspects are omitted, such as the role of aldosterone in the formation and maintenance of ascites and the treatment possibilities of aldosterone antagonists.

In summary, each chapter and each sub-chapter readily could be expanded to a book in themselves and additional topics could be added but, for the purpose it sets out to accomplish, this text will provide the busy clinician a ready reference in his evaluation of the cirrhotic patient and should give him source material to readily understand more current literature on the subject.

Toward the Diagnosis of Congenital Heart Disease

By W. Carleton Whiteside, M.D., Victoria, B. C., Canada. 85 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1960. Price $4.50.

This book contains a brief description of the pathology, symptoms, signs and treatment of the many

forms of congenital heart disease. The first part of the work contains sections concerned with the general principles of pediatric cardiology and a classification of the various entities of congenital heart disease. The bulk of the page space is filled by short chapters each containing a description (in outline form) of one specific malformation, its frequency of occurrence, symptomatology, differentiating characteristics, and general course of therapy. Many statements of Dr. Whiteside's impression, conviction and philosophy are intermingled within these brief outlines. Also, there is a summary section containing tables of the symptomatology and treatment of the more common congenital cardiac defects.

Atlas of Anatomy and Surgical Approaches in Orthopaedic Surgery: The Lower Extremity. Volume II

By Rodolfo Cosentino, M.D., Assistant Professor in Orthopaedic Surgery, University of La Plata, Argentina. 264 pages, illustrated. Springfield, Ill.: Charles C. Thomas, Publisher, 1961. Price $14.00.

The first volume of the *Atlas of Anatomy and Surgical Approaches in Orthopaedic Surgery* by Dr. Cosentino was noted to have great merit for the student of anatomy and for the orthopedic surgeon, since it presented in clear, easily recognizable style the anatomy and the surgical approaches to the upper extremity. The author has now completed Volume Two and there is no question that this combination of volumes makes a very practical and attractive contribution to the medical literature. The photography and brief descriptions which accompany each figure are well done. This book combined with the mate on the upper extremity is applicable to courses of instruction in surgical approaches at all levels of medical experience.

The use of dissection preparations which are illustrated in this atlas serves admirably as the means for review, and they have the advantage of providing a reinforcement of one's original image of anatomy from medical school and postgraduate training.

The Care of Minor Hand Injuries

By Adrian E. Flatt, M.D., Assistant Professor of Orthopedic Surgery, State University of Iowa. 260 pages, illustrated. St. Louis: The C. V. Mosby Company, 1959. Price $9.50.

The so-called minor hand injury occurs frequently and often results in a major loss of hand function. It is important that every injury to the hand be treated with respect. The skill which is required may be obtained only with diligent study and practice. This book offers an immense amount of information which will be useful for all those who treat injuries of the hand. It is sufficiently broad in scope to be considered a good reference book, but its style and presentation make for ready accessibility. The book is highly recommended and will undoubtedly have wide usefulness.

Disc Lesions

By E. J. Crisp, M.D., D.Phys.Med. (Lond.), Consultant Physician Emeritus in Physical Medicine, Guy's Hospital, London. 156 pages. Baltimore: The Williams & Wilkins Company, 1960. Price $3.75.

The sub-title for this book is: "And Other Intervertebral Derangements, Treated by Manipulation Traction and Other Conservative Methods." This new book on "The Back" is authored by a British authority in the field of Physical Medicine and deals with the diagnosis and nonsurgical treatment of common disorders of the back encountered in an office and clinic practice.

Part I is devoted to the general anatomy, physiology and biomechanics of the spine and this section of the book is outstanding. The line drawings and illustrative roentgenograms are excellent and the presentation is clear, concise and accurate. Part II is concerned with therapy and many valuable office procedures are described for painful conditions of the cervical, thoracic and lumbar spine. The section on Manipulation and Traction (Part III), describes many of the manipulations commonly employed by nonmedical practitioners in the United States. The indications and rationale for their use is explained and the specific technic for their performance is given in detail.

Occasional allowances must be made for the difference in British and American terminology. For example, diagnoses of lumbago and brachial neuralgia are not commonly made in this country. Also there are those who will disagree with the practice of prescribing a program of extension exercises following the protrusion of a disk.

This book is a notable addition to our literature on the back and will be of great interest to orthopaedists and physiatrists who desire to employ manipulations in their practice. The section on the anatomy and pathologic biomechanics of the spine is easily the best of its kind.

Clinical Chemistry in Practical Medicine

By D. P. Stewart, D.Sc., Ph.D., and D. M. Dunlop, M.D. Edinburgh and London: E. & S. Livingstone, Ltd., 1958. Price $6.75.

This volume provides the student and practitioner with background information regarding the application of clinical chemistry to the practice of medicine. The introduction outlines a rational approach to the use of clinical laboratory determinations. The concepts of "normal range" of value and standard deviation are briefly discussed. In one chapter, there is a discussion of the proper collection and preservation of samples.

The appendices detail basic analytical methods, many of which are suitable for the physician's office laboratory; tabulations of the normal range of values for the important constituents of urine, blood, and cerebrospinal fluid are also included. Most of the chapters are devoted to various aspects of metabolism, providing basic information leading to the proper use and interpretation of chemical determinations on body fluids in health and disease.

Dynamic Psychiatry in Simple Terms

By Robert R. Mezer, M.D., Assistant Professor of Psychiatry, Boston University Medical School. 162 pages. New York: Springer Publishing Company, 1960. Price $2.75.

Four sections are presented concerning, first, meeting the psychiatric patient; next, development of the normal personality; then, illnesses of the personality and last, the normal life. No new concepts are intro-

duced and the development of each topic is very brief and superficial as though this were a review series of lectures for medical students and nurses. If standard psychiatric concepts had not already been grasped by the reader it is doubtful whether this system of "Dynamic Psychiatry" would be of much value, unless the reader perused the interesting references for recommended reading at the end of each chapter. For the advanced reader in psychiatry who has familiarized himself with standard texts as well as classic references, there is likewise little to be gained from this work. However, many medical or paramedical readers who wish to review as painlessly as possible the important concepts of psychodynamics, especially psychosexual development will find a use for this readable book. Although the terminology and classification may not exactly coincide with what one has been using (terminology used based on the *Diagnostic & Statistical Manual* of the American Psychiatric Association) the patients remain the same and the fundamentals unchanging.

An Atlas of Esophageal Motility in Health and Disease

By Charles F. Code, M.D., Professor of Physiology; Brian Creamer, M.D., Research Assistant, Section of Physiology; Jerry F. Schlegel, B.S., Technical Assistant, Section of Physiology; Arthur M. Olsen, M.D., Associate Professor of Medicine; F. Edmund Donoghue, M.D., Instructor in Medicine; and Howard A. Andersen, M.D., Instructor in Medicine, all of the Mayo Clinic and Mayo Foundation. 132 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $8.50.

Although this atlas presents nothing new, it is an effective compilation of graphic data concerning the physiologic responses of the esophagus in health and certain disease states. It is very well illustrated and has a minimum of extraneous comment. The text may be difficult to interpret for those who are not versed in the technics of recording of intraluminal pressure but the typical recordings which are shown to represent achalasia, diffuse spasm, and scleroderma of the esophagus are clearly well done. Two or three references are listed for each of the disease states described, but no mention is made of the patterns of benign stricture, tumor, inflammatory processes or other abnormalities involving the esophagus. This text can be used as a primer by those interested in teaching the physiology of esophageal motility and probably will find its greatest interest among this group.

Diseases of the Nails

By V. Pardo-Castello, M.D., and Osvaldo A. Pardo, M.D., both formerly of the University of Havana Medical School. Third edition. 277 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1960. Price $8.50.

This compact, well-illustrated volume is now in its third edition, indicative of its interest and use despite the seeming narrowness of its subject. Actually, the nail is visible, readily accessible and, in addition to its own inherent disorders, participates in many systemic illnesses. For anyone interested in the niceties of physical diagnosis as well as dermatology, perusal of this text will be enjoyable. The bibliography of 462 references is current to 1959 and griseofulvin.

One wishes the organization and writing were of a caliber above mere listing and description. The paragraphs are short—often just one sentence—and too frequent. No attempt at synthesis is made, the various lesions simply being mentioned seriatim under broad chapter headings. A comparison with the brief but strikingly well-written section on nails in Pillsbury is disheartening; much of the verbal content of this volume might well have been said in one-tenth the space. A critical attitude is lacking in the acceptance of the variety of syphilitic nail lesions, in the bacteriological discussion accompanying paronychia, and in the nail changes of specific vitamin deficiency. The author will remain unique in finding Hippocratic nails "frequent" in tuberculosis. The nail changes associated with parathyroid disease are not mentioned, and one of the more meaningful systemic associations—Muehrcke's lines of hypoalbuminemia (Brit. M. J. 1:1327, 1956)—has been omitted. Finally, there are a moderate number of printing errors.

Unreserved recommendations cannot be granted. The complete coverage, and frequent and well-reproduced photographs will, however, be of decided interest to the discriminating observer.

Heavy Metals and the Brain

By John N. Cumings, M.D., F.R.C.P., Professor of Chemical Pathology in the University of London at the Institute of Neurology. 155 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $7.00.

It is appropriate, at a time when Wilson's hepatolenticular degeneration has been exciting so much interest among neurologists and biochemists, that the author has been induced to write this volume on heavy metals and the central nervous system. In view of his considerable contribution to our understanding of copper metabolism in hepatolenticular degeneration, it is understandable that his review of this subject would be thorough. The major portion of this volume is devoted to copper and hepatolenticular degeneration, including its historical and clinical features, the Kayser-Fleischer rings, the pathologic features and the recent contributions relating to copper metabolism. The theories of the mechanism underlying hepatolenticular degeneration are discussed at the end of this section. The sections on mercury and lead are brief but sufficiently comprehensive. There is an impressive list of about 900 references, more than 500 being concerned with copper and Wilson's disease.

This monograph is highly recommended to neurologists and biochemists. It will also be of interest to others working in allied fields. It deserves a place in all medical libraries.

Trigeminal Neuralgia, Its History and Treatment

By Byron Stookey, M.D., Professor Emeritus of Clinical Neurological Surgery, and Joseph Ransohoff, M.D., Assistant Professor of Clinical Neurological Surgery, both of the College of Physicians and Surgeons, Columbia University. 339 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $10.75.

This is a surgical oriented monograph on a neurologic disorder whose disabling pain to those afflicted is in inverse proportion to its frequency in the population. Within these limitations, this is a successful presentation of an ancient malady, complete with facsimiles of Andre's 1756 description. The author does a very creditable job on the histology, embryology, anatomy and clinical description of his subject. He briefly and appropriately dismisses medical treatment to go on extensively into the various direct therapeutic measures with discussions on the advantages, permanency and complications of each procedure. That one half of a volume of this length on this subject is devoted to surgery, of necessity ablative, is an impressive reminder of how little we actually know about it. Interested surgeons will find complete directions, and those interested in the differential diagnosis and outlook after surgery will find it well documented.

The Metabolic Basis of Inherited Disease

Edited by John B. Stanbury, M.D., Associate Clinical Professor of Medicine, Harvard Medical School; James B. Wyngaarden, M.D., Associate Professor of Medicine and Biochemistry, Duke University Medical Center; and Donald S. Fredrickson, M.D., Senior Research Staff, National Heart Institute. 1,424 pages. New York: McGraw-Hill Book Company, Inc., 1960. Price $30.00.

This is a remarkably complete volume which includes a great deal of information relating to the clinical, biochemical and genetic aspects of the inborn errors of metabolism. It is only through the collaboration of skilled investigators working in these various areas that such a treatise has been made possible.

After an introductory section on inherited variation and metabolic abnormality and the biochemistry of human genetics, the clinical disorders are discussed in related groups. In a section devoted to diseases which become manifest primarily as abnormalities in metal metabolism, one encounters Wilson's disease, hemochromatosis, periodic paralysis, adynamia episodica hereditaria and pseudohypoparathyroidism. In the section devoted to diseases primarily related to disorders of amino acid metabolism, familial goiter, phenylketonuria, tyrosinosis, alcaptonuria, albinism, primary hyperoxaluria and maple syrup urine disease are described. Each disorder is discussed against a background of the relevant biochemical and metabolic material. An extensive bibliography may be found at the end of each chapter. All of the more recent references are included as well as some of the more classic articles on each subject. This monumental volume is almost 1,500 pages long and will be of great interest as a reference work to physicians in almost any field. One cannot recommend this comprehensive work too highly.

Biochemistry of Human Genetics

Ciba Foundation Symposium, edited by G. E. W. Wolstenholme and Cecilia M. O'Connor. 328 pages. Boston: Little, Brown & Company, 1959. Price $9.50.

This volume is the report of a symposium held in May 1959 at the Naples Zoological Station. The participants were outstanding medical and biologic scientists, and the subjects covered ranged from genetic analysis in man to genetic influences on sense perception, hemoglobin synthesis, plasma protein formation, and immunochemistry. Basic genetic mechanisms were discussed, as were a variety of genetically-induced abnormalities of clinical significance. There is heavy emphasis on protein metabolism and consequently little on carbohydrates or lipids. Nonetheless, the papers and discussions should be of great interest to a wide audience of investigators and clinicians. This symposium volume, appearing in the same year as several other books on human biochemical genetics, is another indication of the great contemporary importance of this field of medical science.

Surgical Philosophy in Mass Casualty Management

By Warner F. Bowers, M.D., Col. M. C., Chief, Department of Surgery, Tripler U. S. Army Hospital, Honolulu; and Carl W. Hughes, M.D., Lt. Col., M. C., Assistant Chief, Department of Surgery, Tripler U. S. Army Hospital. 197 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1960. Price $6.75.

Experience in planning for mass casualty management which has been carried out by the Armed Forces has a clear message to surgeons, administrators and medical students, all of whom will have ample opportunities on a smaller scale to implement and to practice the general concepts which are believed necessary for the management of large disasters. This book is well written; it represents the refinement of many presentations to both medical and paramedical personnel. It is to be recommended both because of its message and the interesting and provocative manner in which it is presented. The style of writing makes this book suitable for all those who are concerned in sufficient organization for medical care in military and civilian situations.

Infectious Diseases of Children

By Saul Krugman, M.D., Professor and Chairman, Department of Pediatrics, New York University School of Medicine; and Robert Ward, M.D., Professor and Head, Department of Pediatrics, University of Southern California School of Medicine, Los Angeles. Second Edition. 387 pages. St. Louis: The C. V. Mosby Company, 1960. Price $13.00.

This is a superior clinical manual whose appearance in a second edition just two years after the first is tribute to its effectiveness as well as progress in the viral area. The strong diagnostic emphasis is reinforced by fairly prolific illustration, including many colored illustrations, and unique schematic diagrams showing the differences in the various infectious rashes a pediatrician must cope with frequently and quickly. The therapeutic discussions may be highly recommended; the universal permeation of antibiotics into every branch of clinical medicine has made many strong men lose their perspective. The authors label antimicrobial trends as such and a definitive recommendation is clearly made by them, avoiding dogmatism without loss of the firmness desired in a specialty text. In no way intended as a complete text of infectious diseases, there is nonetheless a scrupulously thorough coverage of the acute viral syndromes which will be most useful. This book may be recommended as a supplement to adult, as well as child, practice.

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References: 1. DeNyse, D. L.: M. Times 87:1512 (Nov.) 1959.
2. Gruenberg, F.: Current Therap. Res. 2:1 (Jan.) 1960.

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Thyroid Tablets (Armour) are prepared from fresh selected glands, desiccated and standardized by official U.S.P. method to contain 0.2 per cent of iodine in thyroid combination. Thyroid Powder U.S.P. (Armour) is standardized and of uniform potency. USES: Thyroid deficiencies, cretinism, myxedema, nodular goiter (nontoxic), non-nodular goiter. A variety of clinical conditions will respond to the use of Thyroid (Armour) when subclinical hypothyroidism is involved. DOSAGE: ¼ to 5 grains daily as required by clinical condition. Therapeutic effect develops slowly and lasts for two months or longer. Thus the daily dose may be given as a single dose (preferably in the morning) rather than several times daily. Patients treated with thyroid should be continuously under the physician's observation. CONTRAINDICATIONS: Heart disease and hypertension, unless the metabolic rate is low. SUPPLIED: Tablets—bottles of 100, 1000 and larger; potencies of ¼, ½, 1, 2 and 5 grains. Powder—1 oz., 4 oz. and 1 lb. bottles.

ARMOUR PHARMACEUTICAL COMPANY
KANKAKEE, ILLINOIS • *Originators of Listica®*

Recognizing that the exchange of ideas is fundamental to medical progress, Lederle continues its Symposium program with the 10th year of scheduled meetings. Through these Symposia, sponsored by medical organizations with our cooperation, over 50,000 physicians have had the opportunity to hear and question authorities on important advances in clinical medicine and surgery. You have a standing invitation to attend any of these Symposia with your wife, for whom a special program is planned.

ANOTHER YEAR OF SYMPOSIA . . .

PROVIDENCE, RHODE ISLAND
Wednesday, November 1, 1961
The Colony Motor Hotel

HARRISBURG, PENNSYLVANIA
Thursday, November 9, 1961
The Penn Harris Hotel

JACKSONVILLE, FLORIDA
Sunday, November 12, 1961
The Robert Meyer Hotel

ALLENTOWN, PENNSYLVANIA
Wednesday, November 15, 1961
The Americus Hotel

SOMERVILLE, NEW JERSEY
Thursday, November 16, 1961
The Far Hills Inn

NASHVILLE, TENNESSEE
Wednesday, November 29, 1961
Meharry Medical College

EDINBURG, TEXAS
Saturday, December 2, 1961
The Echo Motor Hotel

WACO, TEXAS
Sunday, December 10, 1961
The Holiday Inn

Plans for 1962 already include the following Symposia, with more being arranged:

MOBILE, ALABAMA
Friday, January 5, 1962
The Admiral Semmes Hotel

ST. PAUL, MINNESOTA
January 8, 1962
The Hotel Lowry

PORTLAND, OREGON
Wednesday, January 24, 1962
The Sheraton-Portland Hotel

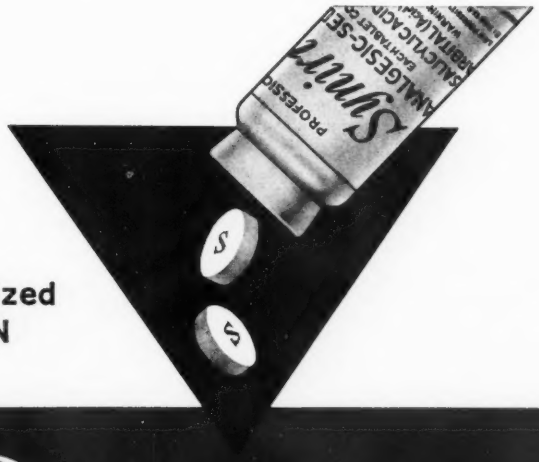
ANCHORAGE, ALASKA
Saturday, February 24, 1962
The Westward Hotel

WINCHESTER, VIRGINIA
Wednesday, March 14, 1962
The Lee-Jackson Hotel

SIOUX CITY, IOWA
Thursday, March 15, 1962
The Sheraton-Martin Hotel

SPOKANE, WASHINGTON
Saturday, June 2, 1962
The Davenport Hotel

Lederle LEDERLE LABORATORIES, a Division of AMERICAN CYANAMID COMPANY, Pearl River, N. Y.



*SYNergized aspIRIN

*Synirin

Acetylsalicylic acid, 5 gr.
Pentobarbital (acid), 1/8 gr.

Simultaneous action beginning promptly lasting four or five hours

◀

Synirin was formulated
for a two-tablet dose for adults
and a one-tablet dose
for children from 5 to 12 years.
May be repeated every four hours
for the relief of pain

Dispensed in bottles of 100 and 1000 tablets

◀

WM. P. POYTHRESS & CO., INC., RICHMOND, VIRGINIA

Manufacturers of ethical pharmaceuticals since 1856

ANNOUNCING

THE TWENTY-FIFTH ANNUAL MEETING

of

THE NEW ORLEANS GRADUATE MEDICAL ASSEMBLY

Conference Headquarters—Roosevelt Hotel

March 12, 13, 14, 15, 1962

GUEST SPEAKERS

E. M. Papper, M.D., New York, N.Y.
Anesthesiology

Edward P. Cawley, M.D., Charlottesville, Va.
Dermatology

Julian M. Ruffin, M.D., Durham, N. C.
Gastroenterology

Carroll L. Witten, M.D., Louisville, Ky.
General Practice

Howard N. Jones, Jr., M.D., Baltimore, Md.
Gynecology

Thomas M. Durant, M.D., Philadelphia, Pa.
Internal Medicine

Maxwell M. Wintrobe, M.D., Salt Lake City, Utah
Internal Medicine

Bernard J. Alpers, M.D., Philadelphia, Pa.
Neurology

Ralph C. Benson, M.D., Portland, Ore.
Obstetrics

Victor A. Byrnes, M.D., St. Petersburg, Fla.
Ophthalmology

John H. Moe, M.D., Minneapolis, Minn.
Orthopedic Surgery

Albert C. Furstenberg, M.D., Ann Arbor, Mich.
Otolaryngology

Jeff Minckler, M.D., Denver, Colo.
Pathology

Lewis L. Coriell, M.D., Camden, N. J.
Pediatrics

Robert D. Moreton, M.D., Fort Worth, Tex.
Radiology

John H. Mulholland, M.D., New York, N. Y.
Surgery

Owen H. Wangensteen, M.D., Minneapolis, Minn.
Surgery

John L. Emmett, M.D., Rochester, Minn.
Urology

Special Wednesday Night Guest

Lectures, symposia, clinicopathologic conferences, round-table luncheons, medical motion pictures, technical exhibits, and entertainment for visiting wives.

(All-inclusive registration fee—$20.00)

THE CLINICAL TOUR TO THE EASTERN MEDITERRANEAN VISITING PARIS, ATHENS, RHODES, CAIRO, LUXOR, JERUSALEM AND TEL AVIV

Leaving March 16 via air and returning April 6, 1962
(Optional extensions may be arranged)

For information concerning the Assembly meeting and the tour write Secretary, Room 105, 1430 Tulane Avenue, New Orleans 12, La.

WHENEVER COUGH THERAPY IS INDICATED

THE COMPLETE Rx FOR COUGH CONTROL

cough sedative | antihistamine
nasal decongestant | expectorant

■ relieves cough and associated symptoms in 15-20 minutes ■ effective for 6 hours or longer ■ promotes expectoration ■ rarely constipates ■ agreeably cherry-flavored

Each teaspoonful (5 cc.) of HYCOMINE* Syrup contains:

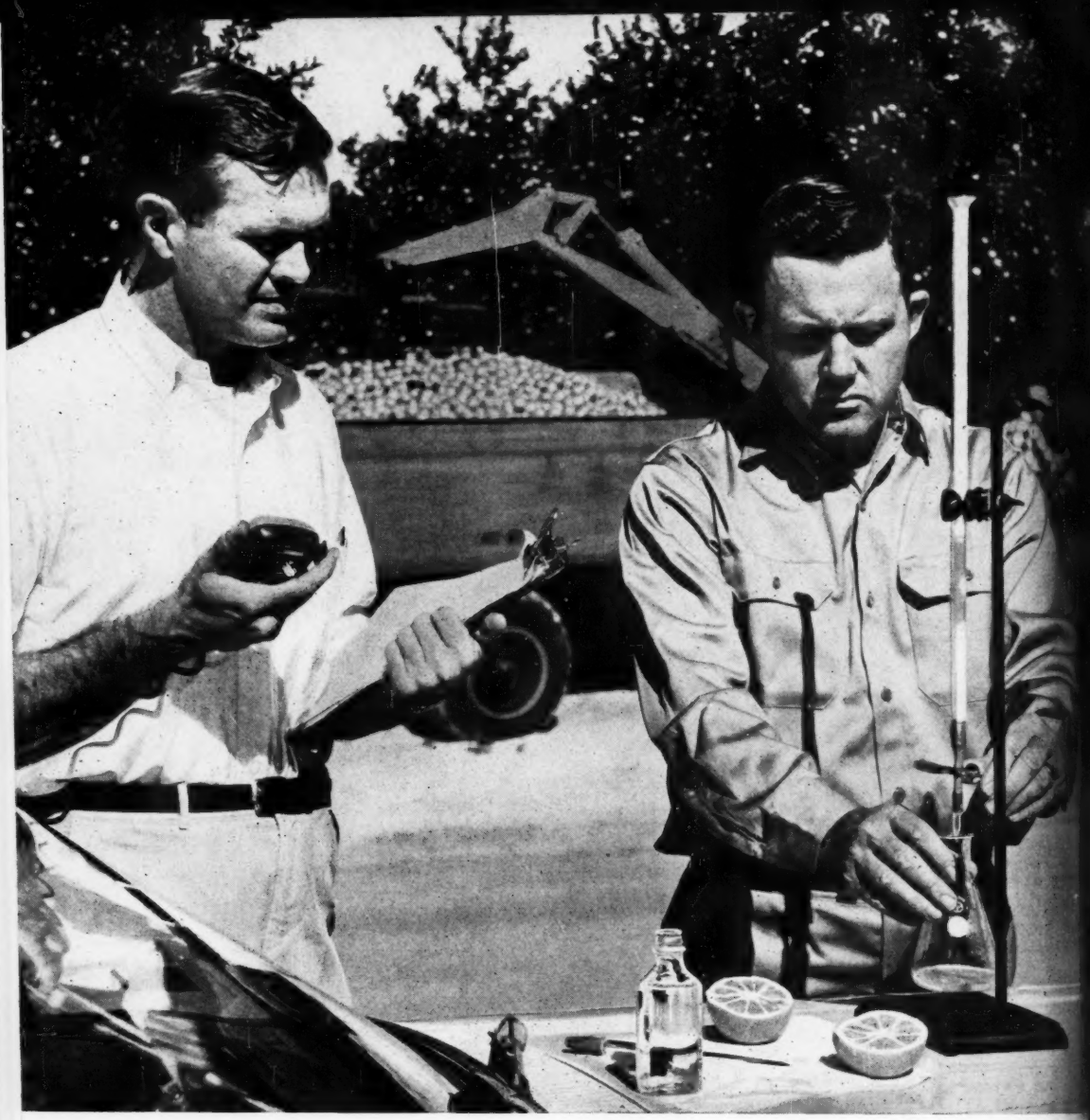
Hycodan*		
Dihydrocodeinone Bitartrate (Warning: May be habit-forming)	5 mg.	6.5 mg.
Homatropine Methylbromide	1.5 mg.	
Pyrilamine Maleate		12.5 mg.
Phenylephrine Hydrochloride		10 mg.
Ammonium Chloride		60 mg.
Sodium Citrate		85 mg.

Average adult dose: One teaspoonful after meals and at bedtime. May be habit-forming. Federal law permits oral prescription.

Literature on request

ENDO LABORATORIES
Richmond Hill 18, New York

*U.S. Pat. 2,630,400



Why Homer Jackson's work is important to you...

Talking on the radio-telephone is Homer Jackson, both a scientist and a buyer for a company processing Florida oranges into frozen juice concentrate.

He has just made a decision that's important to you. He has analyzed some sample oranges from the grove in the background and found that they have the optimal amount of sugar, of acid, and are of the proper texture. (Testing for vitamin C comes later.) Homer Jackson knows that these oranges are of a quality to meet the exacting regulations required by the Florida Citrus Commission.

These standards for quality in citrus products are the highest in the world. This is important to you and your patients because juice made from the best oranges will be nutritionally best for your patients. It will contain abundant amounts of vitamin C and rich, natural fruit sugars.

It's good nutrition to encourage people to drink orange juice. It makes good sense to persuade them to drink orange juice that you *know* tastes good, has the right sugar-acid ratio, and is packed full of nutritionally important vitamin C.

©Florida Citrus Commission, Lakeland, Florida

once again, an active hand in "doing"—

PABALATE®

mutually potentiating nonsteroid antirheumatics

"superior to aspirin"[2] and with a "higher 'therapeutic index'"[1]

In each yellow enteric-coated PABALATE *tablet:*

Sodium salicylate (5 gr.) 0.3 Gm.
Sodium para-aminobenzoate (5 gr.) 0.3 Gm.
Ascorbic acid.....50.0 mg.

When sodium should be avoided—

PABALATE®-SODIUM FREE

In each pink enteric-coated PABALATE-SODIUM FREE *tablet:*

Same formula as PABALATE, with sodium salts replaced by potassium salts.

When conservative steroid therapy is indicated—

PABALATE®-HC

Pabalate with Hydrocortisone

In each light blue enteric-coated PABALATE-HC *tablet:*

Same formula as PABALATE-SODIUM FREE, plus hydrocortisone (alcohol) . . . 2.5 mg.

1. Barden, F. W., et al.: J. Maine M. A. 46:99, 1955.
2. Ford, R. A., and Blanchard, K.: Journal-Lancet 78:185, 1958.

A. H. ROBINS COMPANY, INC., RICHMOND 20, VIRGINIA

Making today's medicines with integrity . . . seeking tomorrow's with persistence

is pharmaceutical advertising really "advertising"?

of course it is, though some have called it "education" . . . not <u>really</u> "advertising."

Of course it's "advertising"... a frankly competitive activity of the American private enterprise system to which this industry belongs. Of course it's "advertising"...created in the hope of getting the physician to note and read; of persuading him, by setting forth proven indications and advantages, to learn about a drug; and of thereby helping him alleviate suffering or cure disease by prescribing it.

"Advertising"? Surely! BUT indisputably different from any other advertising in the world (which is just what has led people to devise various different names for it). For in its proper role it communicates the vital information . . . good, bad, and indifferent . . . and it keeps the physician abreast of each useful new clinical application and each new danger revealed during increasing use of the drug.

There's been a lot of talk about "over-advertising", and there may have been occasional excesses. But consider the potential dangers, in this era of astonishing new drugs, of "under-advertising". . . in view of the complexity of modern drug therapy; the lag of 6 to more than 18 months before the appearance of definitive medical articles on new drugs; and the fact that there is no other source of such comprehensive information about a new agent as the company that ran it through the crucial gauntlet of animal pharmacology and clinical investigation.

This message is brought to you on behalf of the producers of prescription drugs. For additional information, please write Pharmaceutical Manufacturers Association, 1411 K Street, N.W., Washington 5, D.C.

Stop the pain in minutes

When the infection is accompanied by pain, burning or frequency, phenylazo-diamino-pyridine HCl, the local analgesic component, soothes the inflamed urinary mucous membranes. Relief usually comes within a half hour after administration.

Control urinary pathogens

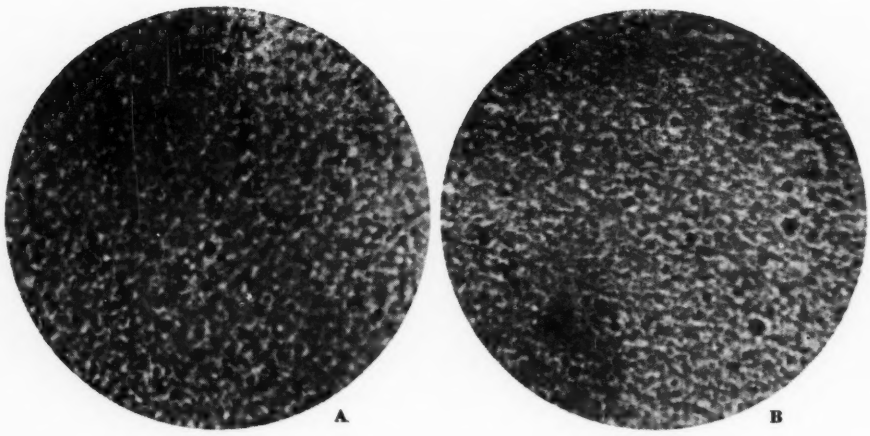
Gantrisin proves effective in most bacterial infections of the genitourinary tract, whether carried by the blood stream or urine. Safety is assured through high solubility.

Gantrisin—"The Quality of Greatness"

Composition: Each tablet contains 500 mg of Gantrisin plus 50 mg of phenylazo-diamino-pyridine HCl. **Usual Adult Dosage:** 2 tablets, 4 times daily. **Warning:** The usual precautions in sulfonamide therapy should be observed. If toxic reactions or blood dyscrasias occur, discontinue administration of the drug. Because Azo Gantrisin contains phenylazo-diamino-pyridine hydrochloride, it is contraindicated in glomerular nephritis, severe hepatitis and uremia. In such cases, Gantrisin should be used alone.

GANTRISIN®—brand of sulfisoxazole

ROCHE
LABORATORIES · Division of Hoffmann-La Roche Inc.



A B

Which is chyle and which is Lipomul I.V.?†

As you know, after digestion, fat passes as an emulsion called chyle through the lacteals into the lymphatics tributary to the thoracic duct, and then into the systemic circulation. Lipomul I. V., like chyle, is a fine milk-white emulsion of fat. Its fat particles approximate those of chyle in size: about *1/7 the diameter of the normal red blood cell.* Because of this minute particle size, like chyle, Lipomul I. V. is *non-irritating to the vein.* The fat provides *8 times more calories* per cc. than does 5% glucose and with markedly increased protein-sparing action. It is *swiftly* and *completely metabolized.* Therefore, when formation of chyle, a major source of calories, is blocked during pre- and post-operative "digestive tract bypass," many surgeons add Lipomul I. V. to their standard fluid and electrolyte regimen to provide the most concentrated source of energy.

†A—Mammalian chyle (highly magnified)
B—Lipomul I. V. (highly magnified)

Formula:

Cottonseed oil	15% w/v
Dextrose anhydrous	4% w/v
Lecithin	1.2% w/v
Oxyethylene oxypropylene polymer	0.3% w/v
Water for injection	q.s.

Supplied in 250 cc. and 500 cc. bottles

Indications and effects

Lipomul I. V., fat emulsion for parenteral use, supplies approximately 400 calories per 250 cc. It is indicated in patients who are unable to take adequate food by mouth for any considerable period of time.

Administration and dosage

Administer only by intravenous route, as follows:

For adults

First 5 minutes	10 drops/minute
Next 25 minutes	40 drops/minute
Then	60 drops/minute

For infants and children

First 5 minutes	5 to 10 drops‡/minute
Next 25 minutes	0.5 to 1 drop per pound/minute
Then	0.5 to 1 drop per pound/minute

‡*1 cc.—approximately 20 drops.*

Precautions and side effects

To administer, use only the recipient set supplied in the package; Lipomul I. V. must not be mixed with transfusions, infusions, or any other parenteral medication, or be given simultaneously through the same tubing. A total of not more than 14 units (500 cc. each), at a rate not exceeding 2 units per day, should be given to any one patient.

Reactions of a "colloid" type may occur, including back or chest pain, dyspnea, severe flushing, or urticaria. There may be delayed chill. Transient fever has also been noted, as have such other minor reactions as nausea, vomiting, abdominal discomfort, headache, mild flushing, dizziness, and some variations in blood pressure and pulse.

When the recommended dosage is exceeded, an "overloading syndrome" may occur characterized by chill, fever, abdominal pain, nausea, vomiting, hepatomegaly, clotting defects, thrombocytopenia, and bleeding, particularly from the gastrointestinal tract.

Lipomul I.V. Upjohn
Trademark, Reg. U. S. Pat. Off.
75th year
THE UPJOHN COMPANY, KALAMAZOO, MICHIGAN

Unquestioned therapeutically

...long established clinically

TRISEM

SUSPENSION **(chocolate-flavored)**

For the many bacterial infections that respond promptly to triple sulfonamide therapy, Trisem presents a preferred formula.

Each 5 cc. contains, in a pleasant, chocolate-flavored vehicle:

Sulfamerazine (microcrystalline) . . . . . 0.167 Gm. (2 3/5 gr.)
Sulfadiazine (microcrystalline) . . . . . 0.167 Gm. (2 3/5 gr.)
Sulfamethazine (microcrystalline) . . . . 0.167 Gm. (2 3/5 gr.)

Each 5 cc. (1 tsp.) provides 0.5 Gm. total sulfonamides.

Each 15 cc. (1 tbsp.) provides 1.5 Gm. total sulfonamides.

ADVANTAGES

- **wide patient acceptability**
- **unquestioned therapeutic value**
- **high index of safety**
- **broad antibacterial spectrum**
- **provides high blood levels promptly**
- **economical for the patient**

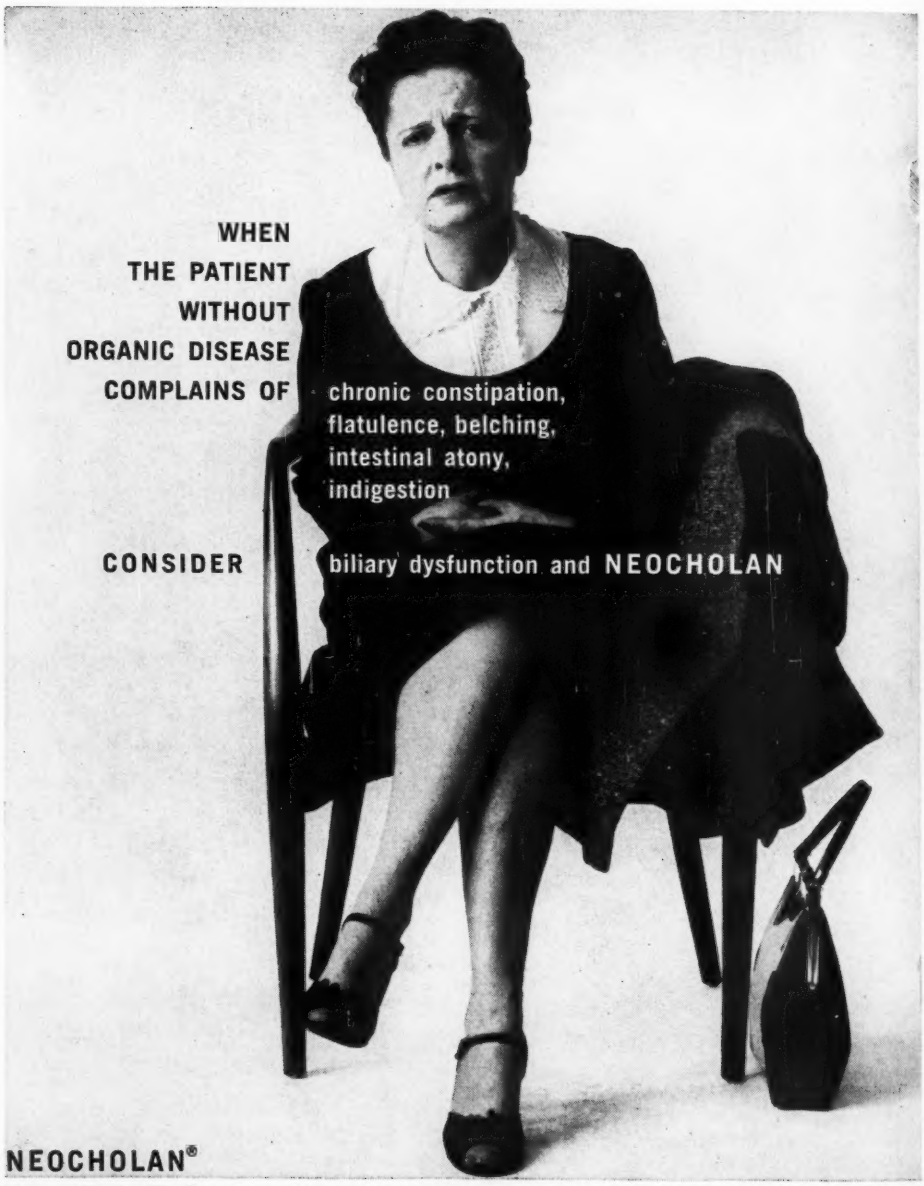
Many physicians prefer to use the sulfonamides to control bacterial infections because resistant organisms rarely develop. Nor, as with some broad spectrum therapy, is there the complication of such after-effects as moniliasis.

PACKAGING: In pint and gallon bottles.

THE S. E. MASSENGILL COMPANY

BRISTOL, TENNESSEE

New York Kansas City San Francisco



NEOCHOLAN®

Your patient will often respond promptly to Neocholan therapy. It greatly increases the flow of thin, nonviscid bile and corrects biliary stasis by flushing the biliary system. It also relaxes intestinal spasm, resulting in an unimpeded flow of bile and pancreatic juice into the small intestine. Neocholan helps to promote proper digestion and absorption of nutrients. It also encourages normal peristalsis by restoring intestinal tone.

Each tablet provides: Dehydrocholic Acid Compound, P-M Co. 265 mg. (Dehydrocholic Acid, 250 mg.); Homatropine methylbromide 1.2 mg.; Phenobarbital 8.0 mg. Supplied in bottles of 100 tablets.

PITMAN-MOORE COMPANY
DIVISION OF THE DOW CHEMICAL COMPANY
INDIANAPOLIS 6, INDIANA

the urethra in postmenopausal urethritis: like "an electric wire with its insulation nearly worn off"*

FURESTROL®

■ restores urethral "insulation" ■ prevents bacterial insult ■ relieves symptoms **Suppositories**

■ estrogenic ■ antibacterial ■ anesthetic ■ gently dilating

In more than 3000 patients, "over 90% have been relieved following treatment"*

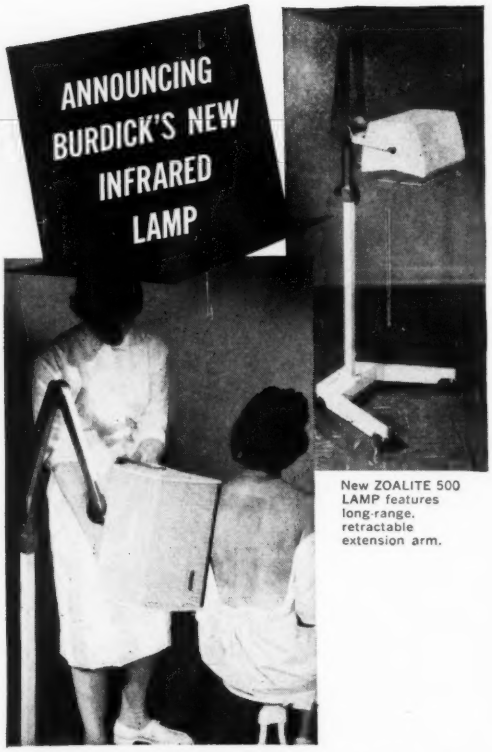
Each FURESTROL Suppository contains diethylstilbestrol 0.0077% (0.1 mg.), FURACIN® (nitrofurazone) 0.2%, and diperodon HCl 2% in a water-dispersible base of glyceryl monolaurate and sorethytan (4) monostearate (Tween 61).

Dosage: One Suppository morning and night for at least 1 week or until symptoms disappear; this may require 2 weeks of therapy.

Supplied: Box of 12, each 1.3 Gm. FURESTROL Suppository hermetically sealed in orchid foil.

*Youngblood, V.H.; Tomlin, E.M., and Williams, J.O.: Gynaecologia (Supp.) *149*:76 (Part 3) 1960.

EATON LABORATORIES, Division of The Norwich Pharmacal Company, NORWICH, NEW YORK

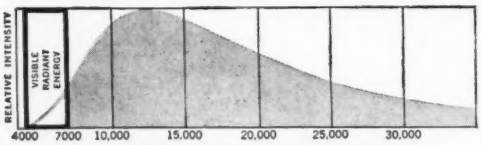


New ZOALITE 500 LAMP features long-range, retractable extension arm.

Radiant energy from the Z-500 Infrared lamp is in the spectral range capable of greater tissue penetration. Its special long-life quartz tube has almost ideal spectral characteristics for therapeutic infrared radiation. (See chart below.)

New equipoise arm permits positioning over widest treatment table. Unique counterbalanced construction holds lamp stationary. The Z-500 also has an Alzak aluminum reflector designed to project radiation evenly over the treatment area. Hot spots are eliminated.

the heart of the new Z-500 is its quartz infrared tube



RELATIVE SPECTRAL DISTRIBUTION IN ANGSTROM UNITS — BURDICK Z-500 LAMP

As will be noted from the above chart, most of its radiant energy is in the range which is capable of the greatest tissue penetration.

SEE THE NEW BURDICK Z-500 ON DISPLAY AT YOUR DEALER'S

Burdick

THE BURDICK CORPORATION
MILTON, WISCONSIN
Branch Offices: New York
Chicago • Atlanta • Los Angeles
Dealers in all principal cities

CLASSIFIED ADVERTISEMENTS

ASSOCIATE WANTED—Internist in Hollywood, Florida desires associate. Office located in new building opposite Memorial Hospital. For details contact: NJL c/o SMJ.

NEVADA—*Senior Psychiatrist*—Salary: Range A—up to $15,408, requires graduation from approved school with one year internship and five years psychiatric experience or residency approved by the A.M.A.; Range B—Salary: up to $16,980, requires same as Range A plus certification by the American Board of Psychiatry and Neurology. Current vacancies exist at the Nevada State Hospital in Reno and in the Community Health Program in Las Vegas. This provides an excellent opportunity for someone desiring location in the center of a recreational and sports area featuring skiing, hunting, fishing, etc. Apply: State Personnel Department, Carson City Nevada.

WANTED—Psychiatrists or general practitioners interested in psychiatry. Prefer board certified or eligible; 2,000-bed, active, fully accredited neuro-psychiatric hospital; full-time staff supplemented with Medical Advisory Committee, consultant and attending physicians. Salary range $10,635.00 to $13,730.00, plus 15% if Board certified. Excellent retirement and fringe benefits. Must be U. S. citizen, graduate of approved medical school, and have current license (any State). Contact Manager, VA Roanoke Hospital, Salem, Virginia.

WANTED—Internist. Board eligible or certified. To be one of three internists in established eight man clinic. Guaranteed salary initially with subsequent partnership. Address Dr. Daniel W. Hayes, Sellers & Sanders Clinic, 4414 Magnolia Street, New Orleans 15, Louisiana.

POSITION WANTED — Internist-Cardiologist desires association. Board eligible after July, 1962 in both internal medicine and cardiology. Now on full time faculty of medical school. Married, one child, 34 years old, veteran. Contact: FLT c/o SMJ.

WANTED — Florida licensed ophthalmologist, board eligible. South Florida location: 45,000 population, unopposed. Contact PRW c/o SMJ. Send curriculum vitae.

MEDICAL NEWS

Continued from page 1325

has received an honorary Doctor of Science Degree from the University of Buffalo.

MISSISSIPPI

Dr. John Frazier, Columbus, is First Vice-President of the Columbus Lions Club.

Dr. Joseph C. Griffing has been named radiologist at Crosby Memorial Hospital in Picayune.

The President of the Columbus Rotary Club is Dr. Henry Holleman, Columbus.

Dr. J. L. Levy, Clarksdale, has been named Medical

Continued on page 72

Geriliquid®

NIACIN AND GLYCINE

PROVIDES SUSTAINED WARMTH OF EXTREMITIES

In patients with impaired peripheral circulation, Geriliquid warms cold hands and feet through rapid, safe vasodilation by niacin, and provides continuing sustained vasodilation and heat radiation by the thermogenic action of glycine.

Other Benefits:

- **Increases ability to walk farther with less pain**
- **Relieves pain, dizziness and faintness**
- **Improves appetite and brightens the mood**

Composition: Each 5 ml. contains: Niacin 75 mg., Glycine 750 mg. in a sherry wine base. Contains Alcohol 5%.

Dosage: One or two teaspoons three times daily before meals.

Supplied: 8 oz. bottles. 72260

LAKESIDE LABORATORIES, INC.
Milwaukee 1, Wisconsin

rhinall

nose drops

Samples on request.

In Nasal Decongestant Therapy when effective shrinkage is desired in treating
Colds • Sinusitis
Allergic Rhinitis

- Rapid and prolonged action
- Small dosage—well tolerated
- Physiological rationale

Prescribed by physicians for over 25 years.

Contains:
Phenylephrine Hydrochloride 0.15%,
'Propadrine' Hydrochloride 0.3%
In an Isotonic Saline Menstruum.

RHINOPTO COMPANY 3905 Cedar Springs • Dallas, Texas

Continued from page 70

Examiner and Surgeon by the city's newly-elected Board of Mayor and Commissioners.

Dr. Guy Robinson, Indianola, has been named a Director of the Indianola Lions Club.

An alderman of Hollandale is Dr. Jack Wilson.

Dr. E. L. Whitfield, Florence, has been named to the Board of Directors of the Rankin County Chamber of Commerce.

The Mississippi State Hospital at Whitfield has added six doctors to its staff. Physicians added are Drs. Charles D. Burgess, William Hilbun, Henry Ray Nail, and Gary A. Sneed. New psychiatrists are Drs. Reginald P. White and Dean Eleftery.

Four new members of the staff of the Greenville General Hospital are: Drs. Verla McAnelly, Hugh Bagby, E. G. Tutor, and Paul Horn.

New members of the Mississippi State Medical Association include: Dr. Robert S. Caldwell, Tupelo; Dr. Joe A. Campbell, Jr., Clarksdale; Dr. James T. Champion, Meridian; Dr. Billy Tommy Collum, Fulton; Dr. Elizabeth G. Dowdy, Jackson; Dr. Frederick C. Grieshaber, Biloxi; Dr. Thomas G. Herrick, Biloxi; Dr. Robert D. Kirk, Jr., Tupelo; Dr. Travis E. Lunceford, Maben; Dr. Errol D. Malvaney, Sanatorium; Dr. George E. Thomas, Gulfport; Dr. Hardy B. Woodbridge, Jr., Jackson; Drs. Ansel Glen Anderson, Jr., and Charles H. Martin, both of Whitfield; and Dr. Charles F. Mitchell, Brandon.

Dr. William Moncure Dabney, Crystal Springs, has been named Editor of the *Journal of the Mississippi State Medical Association*. He had served as Associate Editor since 1958.

Dr. William E. Birdsong has announced his association with the Cosby Clinic in Iuka.

Dr. Kenneth C. Coffelt has been named Pathologist and Laboratory Supervisor for Biloxi Hospital.

The new County Health Officer for Marion and Jefferson Davis Counties is Dr. Vernon L. Terrell, Columbia.

Dr. L. D. Turner, Crystal Springs, is President of the Copiah County Chapter of the University of Mississippi Alumni Association.

Dr. Daniel Trigg has been named Pathologist for Greenwood-Leflore Hospital.

Dr. Dayton E. Whites has announced his association with the Lucedale Medical Clinic.

MISSOURI

Dr. Fernando Tapia, St. Louis, Mental Health Director of the St. Louis County Health Department, has been appointed to head the child psychiatry program at the University of Missouri.

Dr. Robert E. Ryan, St. Louis, is Treasurer of the American Association for the Study of Headache.

The Independence Rotary Club recently installed Dr. Wallace R. Stacy, Independence, as President.

Dr. Carl D. Enna, Kansas City, is President of the Kansas City Council 527 of the Knights of Columbus.

The Radiological Society of North America has elected Dr. John W. Walker, Kansas City, to its Board of Directors.

Continued on page 74

aspirin buffered with the most widely-prescribed antacid...

in long-term administration, as in Arthritis,
when aspirin combined with an antacid is desired:

Specify **Ascriptin**® RORER

the aspirin buffered with the best

To prevent or minimize gastric distress which often accompanies prolonged or high level administration of acetylsalicylic acid, ASCRIPTIN provides aspirin in combination with MAALOX®, the preferred professional antacid. The recognized superiority of MAALOX makes ASCRIPTIN a superior aspirin-antacid, with the virtues of buffered aspirin and with the added distinction of being promoted professionally only.

Indicated wherever salicylates are useful, ASCRIPTIN is particularly suited to the long-term requirements of your arthritic patients.

Supplied: Bottles of 100 and 500 tablets. For severe pain — Capsules ASCRIPTIN with Codeine (codeine phosphate 15 mg.), bottles of 50.

ROHER | WILLIAM H. RORER, INC. PHILADELPHIA, PENNSYLVANIA

TUCKER HOSPITAL, INC.

212 West Franklin St.

RICHMOND, VIRGINIA

A private hospital for diagnosis and treatment of psychiatric and neurological patients. Hospital and out-patient services.

(Organic diseases of the nervous system, psychoneuroses, psychosomatic disorders, mood disturbances, social adjustment problems, involutional reactions and selective psychotic and alcoholic problems.)

DR. JAMES ASA SHIELD DR. WEIR M. TUCKER
DR. GEORGE S. FULTZ, JR. DR. AMELIA G. WOOD

Continued from page 72

The Greater Kansas City chapter of the Myasthenia Gravis Foundation has named a medical advisory board composed of Drs. Richard Helman, Edward G. Kettner, John H. Mayer, Jr., Oscar Pinkster, Ellsworth H. Trowbridge, Jr., and William Q. Wu, all of Kansas City.

The American Association of Industrial Nurses recently appointed Dr. William L. Macon, St. Louis, a member of their medical advisory committee.

New county medical society members in Missouri are: *Callaway,* Dr. Elmer C. Jackson, Fulton; *Cole,* Dr. Joseph P. Russell, Jefferson City; *Greene County,* Drs. Erwin E. Busick, Frank C. Giddings, Harold D. Harvey, Daniel E. Holmes, Louis E. Jorel, and Harwood N. Sturtevant, all of Springfield; *Jackson County,* Drs. Timothy T. Dalton and Andrew McCanse, both of Kansas City; and Drs. Dallas B. Fouts, Sr., and Ivan E. Lloyd, both of Independence; and *St. Louis County,* Drs. Joseph J. Lauber, and Charles B. Powell, both of Florissant; and Dr. J. R. Weber, St. Louis.

New faculty appointments at Washington University School of Medicine include: Dr. Paul E. Lacy, Professor and Head of the Department of Pathology; Dr. Thomas Brugger, Director of the Child Psychiatry Clinics and Assistant Professor of Psychiatry; and Dr. Sarah A. Luse, Associate Professor of Anatomy and Pathology.

The University of Missouri Medical Center has announced two new faculty appointments: Dr. William D. Mayer, Assistant Dean in charge of student affairs;

Continued on page 76

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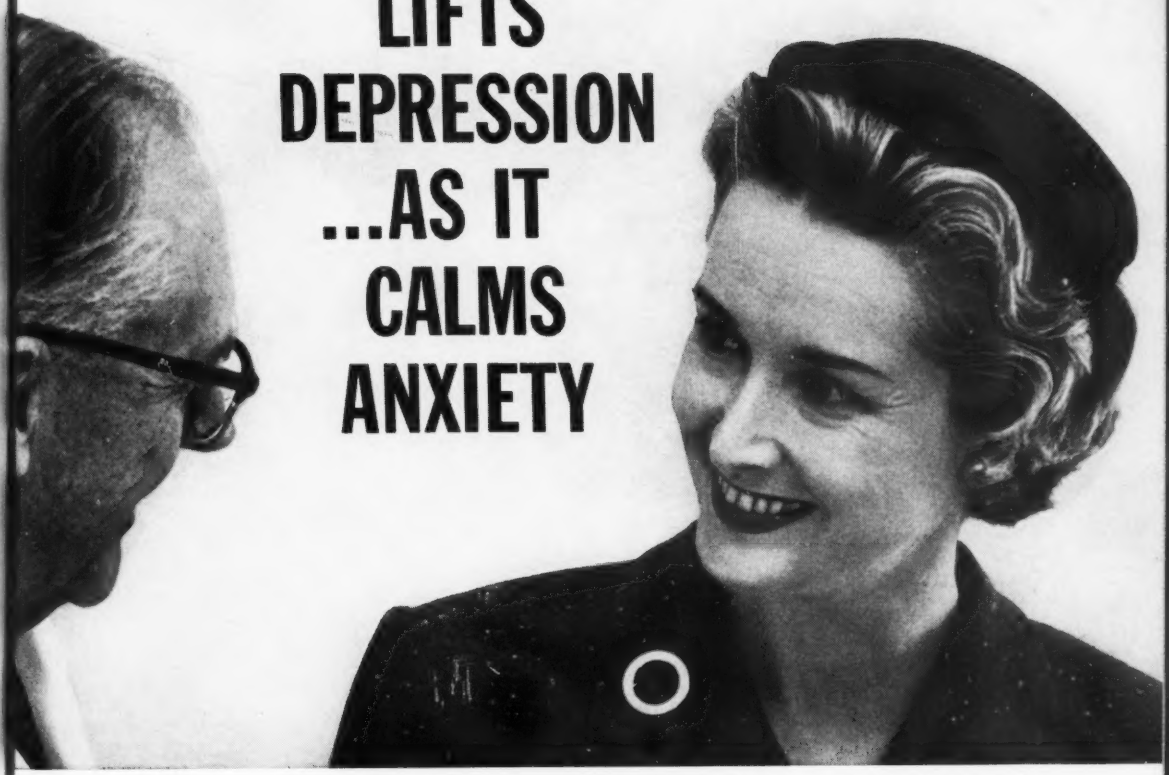

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Continued from page 74

and Dr. Carl J. Marienfeld, Medical Director of the Missouri State Crippled Children's Service and Professor of Preventive Medicine and Public Health.

NORTH CAROLINA

Dr. J. Leonard Goldner, Professor of Orthopedic Surgery at Duke University Medical Center, has been appointed Councilor-Elect of Southern Medical Association for the State of North Carolina. Dr. Goldner succeeds Dr. George D. Wilson, Asheville, and will assume his new duties following SMA's meeting in Dallas, November 6-9.

Faculty appointments at Duke University Medical Center include the following physicians: Dr. F. Stephen Vogel, Professor of Pathology in charge of Neuropathology; Dr. William R. Hudson, Assistant Professor of Otolaryngology; Dr. Stanley M. Kurtz, Assistant Professor of Pathology; and Dr. Benjamin Wittels, Assistant Professor of Pathology.

Three professors at Bowman Gray School of Medicine have been elected to various positions: Dr. Richard L. Burt, Professor of Obstetrics and Gynecology, has been elected to membership in the American Gynecological Society; Dr. Frank R. Johnston, Assistant Professor of Surgery, has been elected to membership in the American Association for Thoracic Surgery; and Dr. Norman M. Sulkin, William Neal Reynolds Professor of Anatomy, has been appointed to the American Biological Research Committee of the International Association of Gerontology.

New members of the Medical Society of the State of North Carolina include: Dr. Arch T. McCoy, Durham; Dr. Jack E. Dunlap, Lumberton; Dr. Devereaux H. Lippitt, New Bern; Dr. Dankwart E. H. Rodler, New Bern; Dr. Ursula Mary Anderson, Raleigh; Dr. Edward L. Groover, Windsor; Dr. Dennis W. Brosnan III, Asheville; Dr. Raeford T. Pugh, Washington; Dr. Charles W. Williams, Charlotte; Dr. Albert McC. Jones, Washington; Dr. Joseph B. Johnston, Jr., Herndon, Virginia; and Dr. Robert B. Hodgson, Reidsville.

SOUTH CAROLINA

Dr. John Crawford Lipsey, Greenville, and Dr. William Frederic Young, Sumter, were certified as specialists by the American Board of Pediatrics, Inc., recently.

Dr. Albert W. Bailey has assumed his duties as pathologist of Tuomey Hospital in Sumter.

Dr. Robert N. Milling, Columbia, has joined the medical staff of the South Carolina State Hospital with assignment to the Admission-Exit Service, Columbia Unit.

TENNESSEE

The Memphis Roentgen Ray Society has the following officers: Dr. Boyer M. Brady, Jr., President; Dr. Marvin M. Keirns, Vice-President; and Dr. Irving K. Ettman, Secretary, all of Memphis.

Dr. Edward McCall Priest has been named Instructor in Medicine at the University of Tennessee College of Medicine.

Three Memphis physicians are Fellows of the American College of Chest Physicians: Drs. G. Daniel Copeland, Charles B. McCall, and I. Frank Tullis.

Appointed as chief of the various services at St. Mary's Hospital in Humboldt were the following physicians: Dr. E. C. Crafton, Chief of Medical Services;

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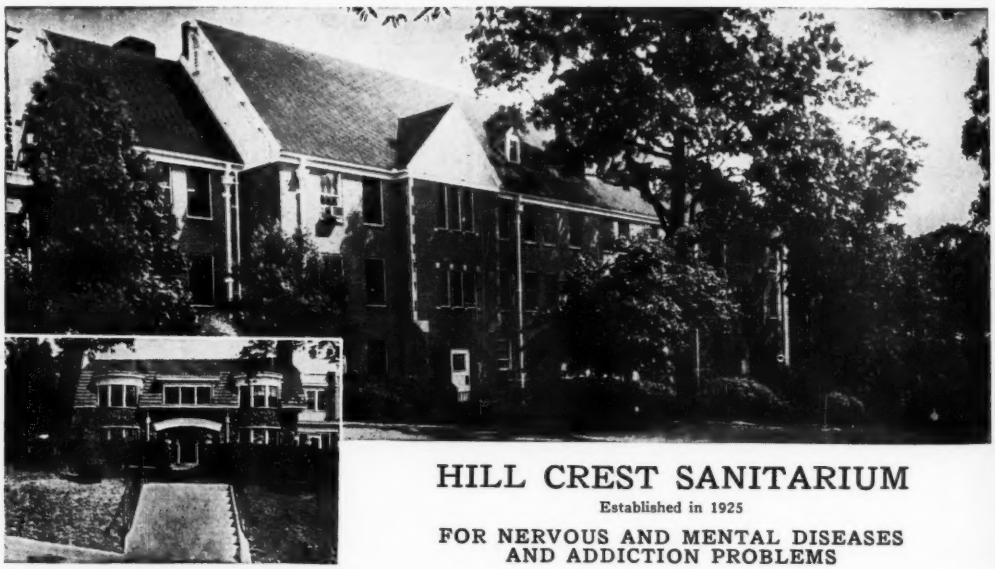

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References:
1. Hahn, David: *Lancet* 2:1018, Nov. 13, 1954. 2. Wagley, P. F.: *Maryland M.J.* 2:183, July, 1953. 3. Jones, W. M.: *Brit. M.J.* 1:1050, May 9, 1953. 4. Jones, W. M.: *Practitioner* 170:185, Feb., 1953.

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Dr. James W. Hall, Chief of Surgery; and Dr. Charles W. Davis, Chief of Obstetrical Services.

Drs. Darrell Mullins and John Overall have joined the staff of Benton Clinic-Hospital in Camden.

Dr. T. R. Ray, Shelbyville, has been appointed to the Tennessee Public Health Council for a 3 year term.

Dr. Coulter S. Young, Manchester, is Chairman of the Manchester Planning and Industrial Commission.

A new member of the staff of McFarland Hospital in Lebanon is Dr. James C. Bradshaw.

Dr. Roy W. Epperson, Athens, has been elected the Eminent Grand Commander of Knights Templar.

Dr. Fred Hooper, Harriman, has been elected County Medical Examiner in Roane County.

Dr. J. V. Havron, South Pittsburg, has been appointed to the Board of Mayor and Commissioners.

The new medical examiner for Gibson County is Dr. Albert H. Fick, Humboldt.

Dr. Hugh J. Morgan, Nashville, has been named to the National Advisory Committee on the Selection of Physicians, Dentists and Allied Specialists.

Dr. Donald Pinkel, formerly of Buffalo, New York, has been appointed Director of Medical Research for St. Jude Hospital in Memphis.

TEXAS

Dr. John P. McGovern, Houston, is Vice-President of the American Association for the Study of Headache. Dr. McGovern is also Vice-Chairman of the Section on Allergy for Southern Medical Association.

Dr. J. Wade Harris, Houston, is Vice-President of the American Proctologic Society.

WEST VIRGINIA

The West Virginia Radiological Society has chosen its new officers: Dr. Hubert A. Shaffer, Morgantown, President; Dr. Rex Dauphin, Parkersburg, Vice-President; and Dr. Karl J. Myers, Philippi, Secretary-Treasurer.

Dr. Charles K. Rath has accepted a position on the staff of the Hinton Hospital in Hinton.

New members of the West Virginia State Medical Association are: Dr. Edward M. Corrill, Beckley; Dr. William E. Brooks, Charleston; and Dr. J. Berrye Worsham, Jr., Pt. Pleasant.

Fellowship certificates were conferred on two West Virginia physicians during the recent meeting of the American College of Chest Physicians. The two new Fellows are Dr. Clark K. Sleeth, Dean of the West Virginia University School of Medicine; and Dr. Charles E. Andrews, Associate Professor of Medicine at the same school.

The West Virginia University Medical Center has announced several additions to its faculty. Dr. Won Bong Hahn is Senior Fellow in Pathology and Medicine; Dr. Grant E. Gauger, Instructor in the Department of Gross and Neurological Anatomy; Dr. William A. Welton, Instructor and Chairman of the newly-formed Division of Dermatology in the Department of Medicine; Dr. Thomas A. Loftus, Professor and Chairman of the Department of Psychiatry; and Dr. Joseph M. Quintero, Assistant Professor and Chairman of the Division of Allergy.

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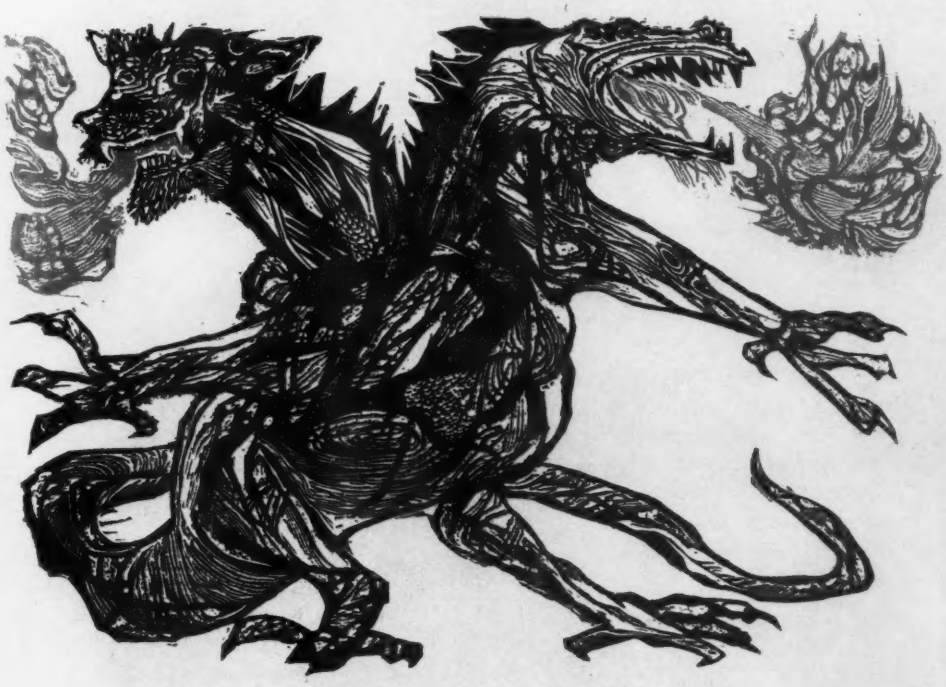

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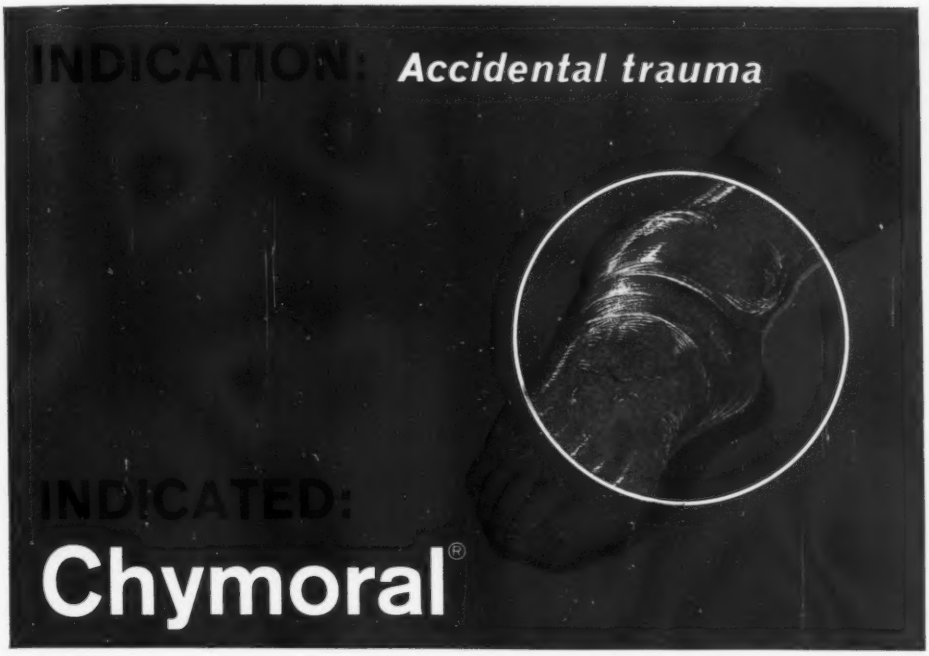

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1. Beck, C., *et al.*: Clin. Med. 7:519, 1960. 2. Teitel, L. H., *et al.*: Indust. Med. 29:150, 1960. 3. Billow, B. W., *et al.*: Southwestern Med. 41:286, 1960. 4. Clinical Reports to the Medical Department, Armour Pharmaceutical Company, 1960. 5. Taub, S. J.: Clin. Med. 7: 2575, 1960.

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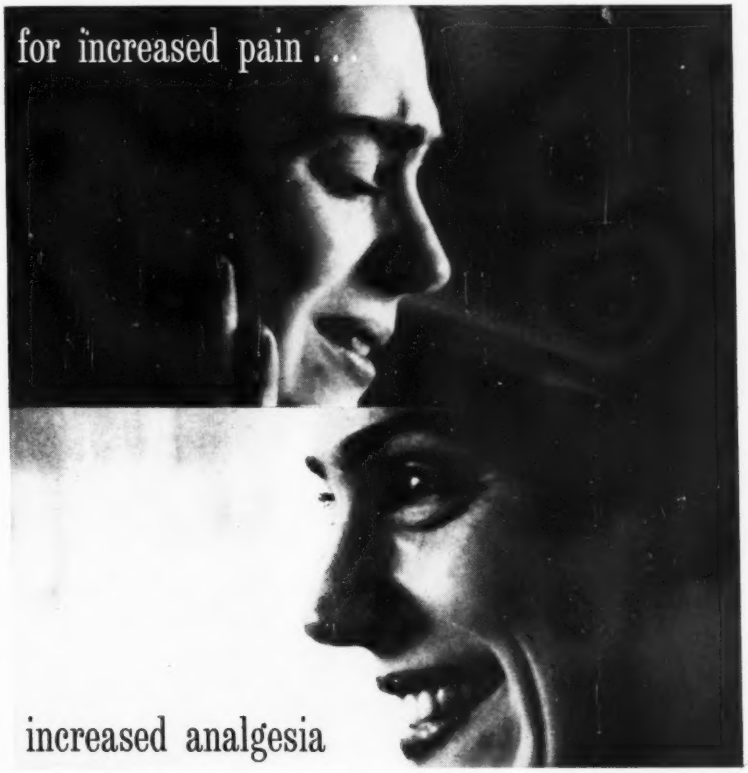

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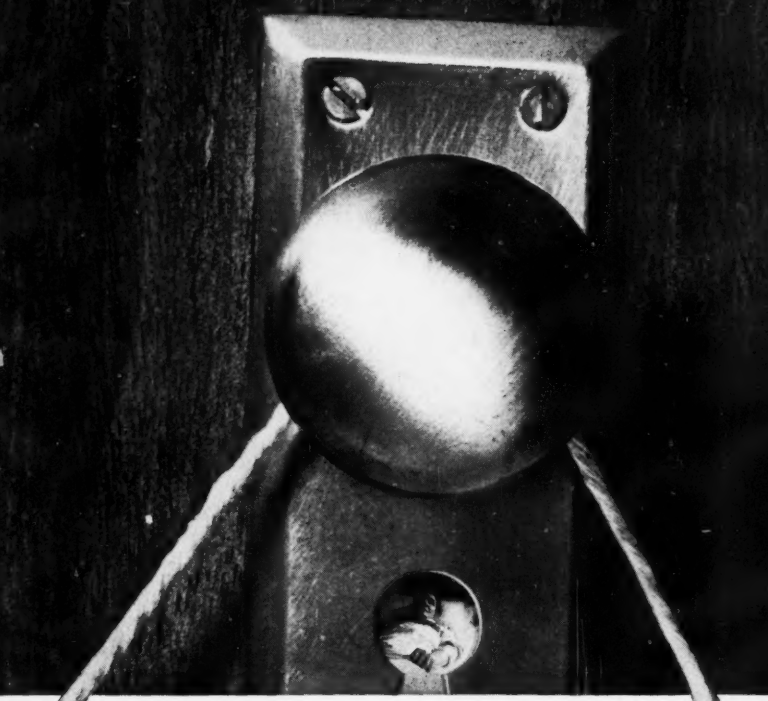

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